PCT/EP2004/011646

EP04/11646

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Patentanmeldung Nr. Patent application No. Demande de brevet n°

03023581.6

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Anmeldung Nr:
Application no.: 03023581.6
Demande no:

Anmeldetag:
Date of filing: 16.10.03
Date de dépôt:

Anmelder/Applicant(s)/Demandeur(s):

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Bezeichnung der Erfindung/Title of the invention/Titre de l'invention:
(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.
If no title is shown please refer to the description.
Si aucun titre n'est indiqué se referer à la description.)

Multispecific deimmunized CD3-binders

In Anspruch genommene Priorität(en) / Priority(ies) claimed /Priorité(s) revendiquée(s)
Staat/Tag/Aktenzeichen/State/Date/File no./Pays/Date/Numéro de dépôt:

Internationale Patentklassifikation/International Patent Classification/
Classification internationale des brevets:

C07K16/00

Am Anmeldetag benannte Vertragstaaten/Contracting states designated at date of filing/Etats contractants désignées lors du dépôt:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL
PT RO SE SI SK TR LI

New European Patent Application
Micromet AG
G 2728 EP

EPO - Munich
41
16. Okt. 2003

Multispecific deimmunized CD3-binders

The present invention relates to a cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain. Furthermore, a nucleic acid sequence encoding a CD3 specific binding construct of the invention is provided. Further aspects of the invention are vectors and host cells comprising said nucleic acid sequence, a process for the production of the construct of the invention and composition comprising said construct. The invention also provides the use of said constructs for the preparation of pharmacutical compositions for the treatment of particular diseases, a method for the treatment of particular diseases and a kit comprising the binding construct of the invention.

Human CD3 denotes an antigen which is expressed on T cells as part of the multimolecular T cell complex and which consists of three different chains: CD3-ε, CD3-δ and CD3-γ. Clustering of CD3 on T cells, e.g, by immobilized anti-CD3 antibodies leads to T cell activation similar to the engagement of the T cell receptor but independent of its clone-typical specificity; see WO 99/54440 or Hoffman (1985) J. Immunol. 135:5-8.

Antibodies which specifically recognize CD3 antigen are described in the prior art, e.g. in Traunecker, EMBO J 10 (1991), 3655-9 and Kipriyanov, Int. J. Cancer 77 (1998), 763-772. Lately, antibodies directed against CD3 have been proposed in the treatment of a variety of diseases. These antibodies or antibody constructs act as either T-cell depleting agents or as mitogenic agents, as disclosed in EP 1 025 854. Human/rodent hybrid antibodies which specifically bind to the human CD3 antigen complex are disclosed in WO 00/05268 and are proposed as immunosuppressive agents, for example for the treatment of rejection episodes following the transplantation of the renal, septic and cardiac allografts. WO 03/04648 discloses a bispecific antibody directed to CD3 and to an ovarian cancer antigen. Furthermore,

Kufer (1997) Cancer Immunol Immunother 45:193-7 relates to a bispecific antibody specific for CD3 and EpCAM for the therapy of minimal residual cancer.

However, prior art antibodies directed against CD3 are derived from non-human sources. This leads to several serious problems when using such anti-CD3 antibodies as part of a therapeutic regimen in humans.

One such problem is "cytokine release syndrome (CRS)". CRS is a clinical syndrome which has been observed following the administration of the first few doses of anti-CD3 antibodies and is related to the fact that many antibodies directed against CD3 are mitogenic. In vitro, mitogenic antibodies directed against CD3 induce T cell proliferation and cytokine production. In vivo this mitogenic activity leads to the large-scale release of cytokines, including many T cell-derived cytokines, within the initial hours after the first injection of antibody. The mitogenic capacity of CD3-specific antibodies is monocyte/macrophage dependent and it involves the production of IL-6 and IL-1β by these cells.

CRS symptoms range from frequently reported mild "flu-like" symptoms to less frequently reported severe "shock-like" reactions (which may include cardiovascular and central nervous system manifestations). Symptoms include, inter alia, headache, tremor, nausea/vomiting, diarrhoea, abdominal pain, malaise and muscle/joint aches and pains, generalized weakness, cardiorespiratory events as well as neuro-psychiatric events. Severe pulmonary oedema has occurred in patients with fluid overload and in those who appeared not to have a fluid overload. Another serious problem hampering the therapeutic use of, especially, murine monoclonal antibodies is the mounting of a humoral immune response against such antibodies, resulting in the production of human anti-mouse antibodies ("HAMAs") (Schroff (1985) Cancer Res.45:879-885, Shawler (1985) J. Immunol. 135:1530-1535). HAMAs are typically generated during the second week of treatment with the murine antibody and neutralize the murine antibodies, thereby blocking their ability to bind to their intended target. The HAMA response can depend on the murine constant ("Fc") antibody regions or/and the nature of the murine variable ("V") regions.

The prior art contains various approaches to reducing or preventing the production of HAMAs by modifying monoclonal antibodies of non-human origin.

One approach to reducing the immunogenicity of such antibodies is by humanization, as for example described in WO 91/09968 and US 6,407,213. In general, humanization entails substitutions of non-human antibody sequences for corresponding human sequences, as for example is the case with CDR-grafting.

Another approach to reducing the immunogenicity of such antibodies is by deimmunization, as for example described in WO 92/10755, WO 00/34317, WO 98/52976, WO 02/079415, WO 02/012899 and WO 02/069232. In general, deimmunization entails carrying out substitutions of amino acids within potential T cell epitopes. In this way, the likelihood that a given sequence will give rise to T cell epitopes upon intracellular protein processing is reduced.

However, humanized and deimmunized antibodies often exhibit a decreased binding affinity with respect to their target as compared to their non-humanized parent antibodies and also often are still somewhat immunogenic in a human host.

Therefore, the technical problem of the present invention was the provision of means and methods for the treatment of and/or the amelioration of tumorous diseases, proliferative disorders as well as B-cell related diseases by induction of T cell mediated immune response. The above-mentioned means and methods should overcome the recited disadvantages of known antibody-based therapies.

The solution to said technical problem is achieved by providing the embodiments characterized in the claims.

Accordingly, the present invention relates to a cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain,
wherein said first domain is deimmunized and comprises a CDR-H1 region, a CDR-H2 region and a CDR-H3 region, said CDR-H3 region comprising an amino acid sequence as depicted in SEQ ID NO 96, 108, 119, 120, 121, 122, 123, 124, 125,

126, or 127; and
wherein said first domain further comprises in its framework H1 the sequence VKK (Val-Lys-Lys) and wherein the transition sequence between framework H1 and CDR-H1 region comprises the sequence Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF; SEQ ID NO: 233).

It was surprisingly found that the above-recited, specific modifications to known CDR regions as well as framework regions and their corresponding transition sequences lead to deimmunized, CD3 specific binding molecules which show reduced immunogenicity but retain their cytotoxic activity compared to original non-deimmunized sequences. This finding was in particular surprising since not all possible deimmunization protocols led to bioactive, functional constructs which show distinct cytotoxic activity; see appended examples. Furthermore, surprisingly the deimmunized cytotoxically active CD3 binding molecules showed increased productivity. In accordance with this invention, specific sequences of non-deimmunized antibodies have been replaced by/modified to the sequences recited here above. In particular, in framework H1 regions original sequence Leu-Ala-Arg (LAR) has been replaced by the sequence Val-Lys-Lys (VKK). Furthermore, the sequence Thr-Ser-Gly-Tyr-Thr-Phe (TSGYTF) comprised in the transition region of framework H1 and CDR-H1 of some non-modified/non-deimmunized CD3-specific antibodies has been modified in accordance with the invention to Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF) (SEQ ID NO.:233) (see Figure 14). A desired, inventive CD3-specific binding construct is characterized as comprising at least two binding specificities whereby a second binding specificity is Ig-derived. Furthermore, said desired constructs are characterized by the specific amino acid sequences shown herein above. As documented in the appended examples the constructs as provided herein still retain bioactivity in their modified/deimmunized form. The examples also document that not all deimmunizations, determined by methods known in the art (WO 92/10755, WO 00/34317, WO 98/52976, WO 02/079415 or WO 02/012899), lead to bioactive molecules; see in particular the examples 2 and 5.

The term "cytotoxically active CD3 binding construct" as used herein relates to a CD3 specific construct capable of binding to human CD3 complex expressed on T cells and capable of inducing elimination/lysis of target cells. Binding of CD3 specific

binders of the CD3/CD3 complex (e.g. antibodies, antibody derivatives or antibody fragments) leads to activation of T cells as known in the art; see WO 99/54440. Accordingly, an inventive construct has to be able to eliminate/lyse target cells in vivo and/or in vitro. Corresponding target cells comprise cells expressing a surface molecule, which is recognized by the second Ig-derived binding domain of the inventive constructs. Such surface molecules are characterized herein below. Cytotoxicity can be detected by methods known in the art and methods as illustrated herein below and in the appended examples. Accordingly, such methods comprise, inter alia, physiological in vitro assays. Such physiological assays may monitor cell death, for example by loss of cell membrane integrity (e.g. FACS based propidium Iodide assay, trypan Blue influx assay, photometric enzyme release assays (LDH), radiometric ^{51}Cr release assay, fluorometric Europium release and CalceinAM release assays). Further assays comprise monitoring of cell viability, for example by photometric MTT, XTT, WST-1 and alamarBlue assays, radiometric ^{3}H-Thd incorporation assay, clonogenic assay measuring cell division activity, and fluorometric Rhodamine^{123} assay measuring mitochondrial transmembrane gradient. In addition, apoptosis may be monitored for example by FACS-based phosphatidylserin exposure assay, ELISA-based TUNEL test, caspase activity assay (photometric, fluorometric or ELISA-based) or analysing changed cell morphology (shrinking, membrane blebbing). It is preferred that cytotoxic activity is analysed by FACS-based measurements of release of fluorescence-based dyes. In such an assay fluorescence labelled cells, which carry a molecule which binds to the second domain of the cytotoxically active bispecific CD3 binding construct of the invention (preferably, NALM-6 cells for CD19 and Kato cells for the EpCAM antigen) are incubated with isolated PBMCs of random donors or with a standardized T-cell line in the presence of the cytotoxically active bispecific CD3 binding construct of the invention. After incubation, the release of the dye from the fluorescent target cells into the supernatant is determined by a spectrofluorimeter. A cytotoxically active deimmunized bispecific CD3 binding construct of the present invention is characterized by comparing values obtained by measuring the bioactivity of a similar construct which is not deimmunized or has no specificity to the target cells.

The term "binding to/interacting with" as used in the context with the present invention defines a binding/interaction of at least two "antigen-interaction-sites" with

each other. The term "antigen-interaction-site" defines, in accordance with the present invention, a motif of a polypeptide which shows the capacity of specific interaction with a specific antigen or a specific group of antigens. Said binding/interaction is also understood to define a "specific recognition". The term "specifically recognizing" means in accordance with this invention that the antibody molecule is capable of specifically interacting with and/or binding to at least two amino acids of each of the human target molecule as defined herein. Antibodies can recognize, interact and/or bind to different epitopes on the same target molecule. Said term relates to the specificity of the antibody molecule, i.e. to its ability to discriminate between the specific regions of the human target molecule as defined herein. The specific interaction of the antigen-interaction-site with its specific antigen may result in an initiation of a signal, e.g. due to the induction of a change of the conformation of the antigen, an oligomerization of the antigen, etc. Thus, specific motif in the amino acid sequence of the antigen-interaction-site and the antigen bind to each other as a result of their primary, secondary or tertiary structure as well as the result of secondary modifications of said structure.

The term "specific interaction" as used in accordance with the present invention means that the CD3 specific binding construct of the invention does not or essentially does not cross-react with (poly)peptides of similar structures. Accordingly, the construct of the invention specifically binds to/interacts with human CD3 and is capable, due to its second, Ig-derived domain to interact with specific, selected other compounds, antigens, cell surface markers, tumor markers, etc. Specific examples of such molecules against which said second, Ig-derived domain is directed are given herein below.

Cross-reactivity of a panel of constructs under investigation may be tested, for example, by assessing binding of said panel of bispecific single chain constructs under conventional conditions (see, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988 and Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, 1999) to the (poly)peptide of interest as well as to a number of more or less (structurally and/or functionally) closely related (poly)peptides. Only those constructs (i.e.antibodies, (bispecific) scFvs and the like) that bind to the (poly)peptide/protein of interest but do not or do not essentially bind to any of the other (poly)peptides which are preferably expressed by the same tissue as the (poly)peptide of interest, e.g. by the cells of the heart

tissue, are considered specific for the (poly)peptide/protein of interest and selected for further studies in accordance with the method provided herein and illustrated in the appended examples. These methods may comprise, inter alia, binding studies, blocking and competition studies with structurally and/or functionally closely related molecules. These binding studies also comprise FACS analysis, surface plasmon resonance (SPR, e.g. with BIAcore®), analytical ultracentrifugation, isothermal titration calorimetry, fluorescence anisotropy, fluorescence spectroscopy or by radiolabeled ligand binding assays. Furthermore, physiological assays, like cytotoxic assays (as illustrated in the examples) and assays mentioned above may be performed. Accordingly, examples for the specific interaction of an antigen-interaction-site with a specific antigen may comprise the specificity of a ligand for its receptor. Said definition particularly comprises the interaction of ligands which induce a signal upon binding to its specific receptor. Examples for corresponding ligands comprise cytokines which interact/bind with/to its specific cytokine-receptors. Also particularly comprised by said definition is the binding of an antigen-interaction-site to antigens such as antigens of the selectin family, integrins and of the family of growth factors like EGF. An other example for said interaction, which is also particularly comprised by said definition, is the interaction of an antigenic determinant (epitope) with the antigenic binding site of an antibody.

The term "binding to/interacting with" relates not only to a linear epitope but may also relate to a conformational epitope, a structural epitope or a discontinuous epitope consisting of two regions of the human target molecules or parts thereof. In context of this invention, a conformational epitope is defined by two or more discrete amino acid sequences separated in the primary sequence which come together on the surface of the molecule when the polypeptide folds to the native protein (Sela, (1969) Science 166, 1365 and Laver, (1990) Cell 61, 553-6).

The term "discontinuous epitope" means in context of the invention non-linear epitopes that are assembled from residues from distant portions of the polypeptide chain. These residues come together on the surface when the polypeptide chain folds into a three-dimensional structure to constitute a conformational/structural epitope.

The constructs of the present invention are also envisaged to specifically bind to/interact with a conformational/structural epitope(s) composed of and/or comprising the two regions of the human CD3 complex described herein or parts thereof as

disclosed herein below.

Accordingly, specificity can be determined experimentally by methods known in the art and methods as disclosed and described herein. Such methods comprise, but are not limited to Western blots, ELISA-, RIA-, ECL-, IRMA-tests and peptide scans.

The term "Ig-derived second binding domain" relates to an "immunoglobulin-derived domain" , specifically to an antibody or fragments thereof, to single chain antibodies, to synthetic antibodies, to antibody fragments, such as Fab, a $F(ab_2)'$, Fv or scFv fragments etc, or a chemically modified derivative of any of these. These antibodies molecules may be derived from different species or may be of chimeric origin. Most preferably (as documented herein below), said Ig-derived second domain comprised in the CD3 specific binding construct of the invention is a scFv. Antibodies, antibody constructs, antibody fragments, antibody derivatives (all being Ig-derived) to be employed in accordance with the invention or their corresponding immunoglobulin chain(s) can be further modified using conventional techniques known in the art, for example, by using amino acid deletion(s), insertion(s), substitution(s), addition(s), and/or recombination(s) and/or any other modification(s) known in the art either alone or in combination. Methods for introducing such modifications in the DNA sequence underlying the amino acid sequence of an immunoglobulin chain are well known to the person skilled in the art; see, e.g., Sambrook (1989), loc. cit. The term "Ig-derived domain" particularly relates to (poly)peptide constructs comprising at least one CDR. Fragments or derivatives of the recited Ig-derived domains define (poly)peptides which are parts of the above antibody molecules and/or which are modified by chemical/biochemical or molecular biological methods. Corresponding methods are known in the art and described inter alia in laboratory manuals (see Sambrook et al.; Molecular Cloning: A Laboratory Manual; Cold Spring Harbor Laboratory Press, 2nd edition 1989 and 3rd edition 2001; Gerhardt et al.; Methods for General and Molecular Bacteriology; ASM Press, 1994; Lefkovits; Immunology Methods Manual: The Comprehensive Sourcebook of Techniques; Academic Press, 1997; Golemis; Protein-Protein Interactions: A Molecular Cloning Manual; Cold Spring Harbor Laboratory Press, 2002).

The term "deimmunized" as used herein relates to the above-identified first domain of the inventive CD3 binding construct, wherein said first domain is modified compared

to an original wild type construct by rendering said wild type construct non-immunogenic or less immunogenic in humans. Wild type constructs according to the invention relate to antibodies or parts thereof (like frameworks and/or CDRs) of non-human origin. Corresponding examples are antibodies or fragments thereof as described in US 4,361,549 or WO 99/54440. The term "deimmunized" also relates to constructs, which show reduced propensity to generate T cell epitopes. In accordance with this invention, the term "reduced propensity to generate T cell epitopes" relates to the removal of T-cell epitopes leading to specific T-cell activation. Furthermore, reduced propensity to generate T cell epitopes means substitution of amino acids contributing to the formation of T cell epitopes, i.e. substitution of amino acids, which are essential for formation of a T cell epitope. In other words, reduced propensity to generate T cell epitopes relates to reduced immunogenicity or reduced capacity to induce antigen independent T cell proliferation. In addition, reduced propensity to generate T cell epitopes relates to deimmunisation, which means loss or reduction of potential T cell epitopes of amino acid sequences inducing antigen independent T cell proliferation. According to the invention, a CD3 binding region, which has reduced propensity to generate T cell epitopes is less or preferably non immunogenic compared to non-deimmunized molecule but which has still retained its capacity to binding to CD3, i,e. a low/non immunogenic antibody construct binding to CD3. The term "T cell epitope" relates to short peptide sequences which can be released during the degradation of peptides, polypeptides or proteins within cells and subsequently be presented by molecules of the major histocompatibility complex (MHC) in order to trigger the activation of T cells; see inter alia WO 02/066514. For peptides presented by MHC class II such activation of T cells can then give rise to an antibody response by direct stimulation of T cells to produce said antibodies.

Accordingly, a deimmunized first domain specifically binding to a human CD3 comprises at least the above mentioned CDR-H3 located between framework H3 and H4, wherein said first binding domain shows a reduced propensity to generate T-cell epitopes compared to a non-deimmunized first domain comprising the unchanged wt-CDR-H3 located between framework H3 and H4. Furthermore, said deimmunized first domain comprises at least in the transition region of the framework H1 and CDR-H1 the above mentioned sequence motif which provides a reduced propensity to generate T-cell epitopes compared to a non-deimmunized first domain comprising the unchanged wt-H1 transition region of the framework H1 and CDR-H1.

"Reduced propensity to generate T-cell epitopes" and/or "deimmunization" may be measured by techniques known in the art. Preferably, de-immunization of proteins may be tested in vitro by T cell proliferation assay. In this assay PBMCs from donors representing > 80 % of HLA-DR alleles in the world are screened for proliferation in response to either wild type or de-immunized peptides. Ideally cell proliferation is only detected upon loading of the antigen-presenting cells with wild type peptides. Alternatively, one may test deimmunization by expressing HLA-DR tetramers representing all haplotypes. These tetramers may be tested for peptide binding or loaded with peptides substitute for antigen-presenting cells in proliferation assays. In order to test if de-immunized peptides are presented on HLA-DR haplotypes, binding of e.g. fluorescence-labeled peptides on PBMCs can be measured. Furthermore, de-immunization can be proven by determining whether antibodies against the de-immunized molecules have been formed after administration in patients. A particular preferred method is a T-cell proliferation assay as, inter alia, shown in appended example 6.

Preferably, antibody derived molecules are deimmunized in the framework regions and most of the CDR regions are not modified in order to generate reduced propensity to induce T cell epitope so that the binding affinity of the CDR regions is not affected. Even elimination of one T cell epitope results in reduced immunogenicity. Preferably, the molecule is deimmunized in the CDR2 region of the VL chain, more preferably in the CDR2 region of the VH chain, even more preferably in the CDR1 region of the VL chain, even more preferably in the CDR1 region of the VH chain, more preferably in the framework region (FR) of the VL chain and most preferably in the framework region (FR) of the VH chain.

The term "CDR" as employed herein relates to "complementary determining region", which is well known in the art. The CDRs are parts of immunoglobulins and T cell receptors that determine the specificity of said molecules and make contact with specific ligand. The CDRs are the most variable part of the molecule and contribute to the diversity of these molecules. There are three CDR regions CDR1, CDR2 and CDR3 in each V domain. CDR-H depicts a CDR region of a variable heavy chain and CDR-L relates to a CDR region of a variable light chain. H means the variable heavy chain and L means the variable light chain. The CDR regions of an Ig-derived region may be determined as described in Kabat (1991). Sequences of Proteins of

Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services, Chothia (1987). J. Mol. Biol. 196, 901-917 and Chothia (1989) Nature, 342, 877-883.

In general CDR-L1 consists of 10-17 amino acid residues, starts approximately at amino acid residue 24 of the full VL region of an Ig-derived sequence and the residue Cys precedes the CDR-L1. Preferably, the residue Trp follows CDR-L1. CDR-L2 starts preferably, 16 amino acid residues after CDR-L1 and consists preferably of 7 residues. Preferably, the amino acid residues Ile-Tyr, but also, Val-Tyr, Ile-Lys, Ile-Phe precede CDR-L2. CDR-L3 starts, preferably, 33 amino acid residues after CDR-L2 and consists, preferably, of 7-11 residues. CDR-L3 follows, preferably, the residue Cys and, preferably, the residues Phe-Gly-Xaa-Gly follow directly CDR-L3. CDR-H1 consists of, preferably, 10-12 residues and starts, preferably, approximately at residue 26 from the beginning of the VH region. Preferably, the residue Trp follows CDR-H1. CDR-H2 starts, preferably, 15 amino acid residues after the end of CDR-H1 and consists, preferably, of 16 to 19 residues. Preferably, residues Lys/Arg-Leu/Ile/Val/Phe/Thr/Ala-Thr/Ser/Ile/Ala follow CDR-H2. CDR-H3 starts 33 amino acid residues after CDR-H2 and has a length of 3-25 amino acid residues. CDR-H3 follows the sequence Cys-Xaa-Xaa (preferably Cys-Ala-Arg) and the residues Trp-Gly-Xaa-Gly follow CDR-H3. The structure of CDR region has been described in http://www.bioinf.org.uk/abs/.

The above recited CDR-H1 and CDR-H2 regions are derived from antibody molecules which are capable of specifically binding to/interacting with human CD3. Such CD3 specific antibody are known in the art and comprise in particular the monoclonal antibodies OKT-3, TR-66 or X35-3, VIT3, BMA030 (BW264/56), CLB-T3/3, CRIS7, YTH12.5, F111-409, CLB-T3.4.2, TR-66, WT32, SPv-T3b, 11D8, XIII-141, XIII-46, XIII-87, 12F6, T3/RW2-8C8, T3/RW2-4B6, OKT3D, M-T301, SMC2, F101.01, UCHT-1 or WT-31. All the mentioned anti-CD3 antibodies are human specific and in accordance with this invention it is possible to combine various CDR regions, in particular CDRH regions of the antibodies.

In a more preferred embodiment, said CDR-H1 and CDR-H2 regions of said CD3 specific domain with reduced propensity to generate T cell epitopes are derived from

the antibody construct described in WO 99/54440. Even more preferred (and as illustrated in the appended examples) said CDR-H1 and CDR-H2 regions, as well as the CDR-H3 region, are derived from an antibody/antibody derivative with specificity for the CD3 molecule described by Traunecker (1991), EMBO J. 10, 3655-3659. In accordance with this invention, said CDR-H1, CDR-H2 and CDR-H3 regions are derived from antibodies/antibody derivatives and the like which are capable of specifically recognizing the human CD3-ε chain in the context of other TCR subunits, e.g. in mouse cells transgenic for human CD3-ε chain. These transgenic mouse cells express human CD3-ε chain in a native or near native conformation.

In accordance with this invention, a framework region relates to a region in the V domain (VH or VL domain) of immunoglobulins and T-cell receptors that provides a protein scaffold for the hypervariable complementarity determining regions (CDRs) that make contact with the antigen. In each V domain, there are four framework regions designated FR1, FR2, FR3 and FR4. Framework 1 encompasses the region from the N-terminus of the V domain until the beginning of CDR1, framework 2 relates to the region between CDR1 and CDR2, framework 3 encompasses the region between CDR2 and CDR3 and framework 4 means the region from the end of CDR3 until the C-terminus of the V domain; see, inter alia, Janeway, Immunobiology, Garland Publishing, 2001, 5th ed. Thus, the framework regions encompass all the regions outside the CDR regions in VH or VL domains. Furthermore, the term "transition sequence between a framework and a CDR region" relates to a direct junction between the framework and CDR region. In particular, the term "transition sequence between a framework and a CDR region" means the sequence directly located N- and C-terminally of the CDR regions or amino acids surrounding CDR regions. Accordingly, frameworks may also comprise sequences between different CDR regions. The person skilled in the art is readily in a position to deduce from a given sequence the framework regions, the CDRs as well as the corresponding transition sequences; see Kabat (1991) Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services, Chothia (1987). J. Mol. Biol. 196, 901-917 and Chothia (1989) Nature, 342, 877-883..

A preferred cytotoxically active CD3 specific binding construct of the invention further

comprises in said first domain a framework H3 comprising the sequence Met-Glu-Leu-Ser (MELS; SEQ ID NO:234). Even more preferred is an inventive construct which comprises in said first domain a framework H3 comprising the sequence Ile-Thr-Thr-Asp-Lys (ITTDK; SEQ ID NO: 235).

In accordance with the present invention, the first domain of the inventive construct specifically binding to/interacting with human CD3 and having a reduced propensity to generate T cell epitopes, comprises a CDR-H1, CDR-H2 and CDR-H3 regions as defined herein and, in a preferred embodiment, VH-frameworks (frameworks 1, 2, 3, 4) as defined above, in particular as shown in any one of SEQ ID NOs.: 152 or 153, 156 or 157, 160 or 161 and/or 164 or 165. Therefore, the CD3 specific binding construct of the invention comprises a first domain which specifically binds to human CD3 and comprises a framework region 1 as shown in SEQ ID NO. 152 or 153, a framework region 2 as shown in SEQ ID NO. 156 or 157, a framework region 3 as shown in SEQ ID NO. 160 or 161 and/or a framework region 4 as shown in SEQ ID NO. 164 or 165.

In a particularly preferred embodiment of the invention, the cytotoxically active deimmunized CD3 specific binding construct comprises in its first domain (a) a CDR-H1 as depicted in SEQ ID NO 88; and (b) a CDR-H2 as depicted in SEQ ID NO 90 or 92.

Accordingly, the modified CDR-H1 and CDR-H2 regions lead to a reduced propensity to generate T cell epitopes and are derived from an CD3-ε chain specific antibody. Most preferably in accordance with this invention said (parental) antibodies should be capable of specifically binding epitopes reflecting the native or near native structure or a conformational epitope of human CD3 presented in context of the TCR complex.

Preferably, the CD3 specific binding construct of the invention comprises a VH-region as depicted in SEQ ID NO.74 or 76. SEQ ID NO:74 shows an illustrative deimmunized variable heavy region and, similarly, SEQ ID NO:76 shows an illustrative deimmunized variable heavy region.

Preferably, the inventive CD3 specific binding construct comprises a CDR-L1 as depicted in SEQ ID NO. 98 or 100, a CDR-L2 as depicted in SEQ ID NO.102 and/or a CDR-L3 as depicted in SEQ ID NO.104.

The CD3 specific binding construct of the invention comprises, in a preferred embodiment, a VL region in its CD3-specific portion, wherein said VL region is selected from the group consisting of SEQ ID NO 78 , SEQ ID NO 80, SEQ ID NO 82 and SEQ ID NO 112. VL1 as characterized in SEQ ID NO.:78, VL2 as characterized in SEQ ID NO.:80 and VL 3 as characterized in SEQ ID NO.:82 relate to full deimmunized VL regions in accordance with this invention, and they may be used in various combinations with the above described VH regions. Yet, it is also envisaged that the non-deimmunized VL region may be combined, in accordance with the invention, with deimmunized VH regions defined above. A corresponding non-deimmunized VL-region preferably employed in an cytotoxically active CD3 binding construct of the invention, is shown in SEQ ID NO.: 112. Accordingly, not only heavy chain part of the above recited "first domain" of the inventive CD3 construct may be modified to have a reduced propensity to generate T cell epitopes. It is also envisaged that said domain comprises the corresponding variable light chain parts. SEQ ID NOs. 78, 80, and 82, for example, depict deimmunized VL1, VL2 and VL3 regions of the CD3 binding part of a construct disclosed in WO 99/54440.

As mentioned above, the CD3 specific binding construct of the invention, most preferably, comprises an Ig-derived second domain which is a scFv. Accordingly, in a most preferred embodiment of the present invention, a deimmunized, bispecific single chain antibody construct is provided with one specificity for human CD3 and a further specificity which is mediated by a second scFv, directed against/capable of interacting with a further molecule/compound. These further molecules/compounds may comprise cell surface molecules, tumor markers, tumor antigens and the like. Such further compounds/molecules are exemplified herein below and specific constructs are also given and provided in the appended examples.

The term "bispecific single chain antibody construct" relates to a construct comprising two antibody derived binding domains, preferably scFvs. One of said binding domains consists of variable regions (or parts thereof) of an antibody, antibody

fragment or derivate thereof, capable of specifically binding to/interacting with human CD 3 antigen (target molecule 1). The second binding domain consists of variable regions (or parts thereof) of an antibody, antibody fragment or derivative thereof, capable of specifically binding to/interacting with another (human) antigen (target molecule 2) as defined below. Accordingly, said second binding domain is, in accordance with this invention, the Ig-derived second domain recited above which comprises an antigen-interaction-site with specificity for a cell surface molecule and/or a tumor specific marker. Said two domains/regions in the bispecific construct, preferably said bispecific single chain antibody construct, are preferably covalently connected to one another as a single chain. This connection can be effected either directly (domain 1 [specific for human CD3 antigen, comprising a reduced propensity to generate T cell epitopes and comprising CDR-regions or CDR-regions and framework regions as defined above] – domain 2 [specific for a cell surface molecule and/or a tumor specific marker] or domain 1 [specific for a cell surface molecule and/or a tumor specific marker] – domain 2 [specific for human CD3 antigen, comprising a reduced propensity to generate T cell epitopes and comprising CDR-regions or CDR-regions and framework regions as defined above]) or through an additional polypeptide linker sequence (domain1 – linker sequence – domain2). In the event that a linker is used, this linker is preferably of a length and sequence sufficient to ensure that each of the first and second domains can, independently from one another, retain their differential binding specificities. As mentioned above and as documented in the appended examples, preferably, the CD3 specific binding construct comprising at least two domains as defined herein is a "bispecific single chain antibody construct", most preferably a bispecific single chain Fv (scFv). It is in particular envisaged that said construct is employed in context of a pharmaceutical composition. Bispecific single chain molecules are known in the art and are described in WO 99/54440, Mack, J. Immunol. (1997), 158, 3965-3970, Mack, PNAS, (1995), 92, 7021-7025, Kufer, Cancer Immunol. Immunother., (1997), 45, 193-197, Löffler, Blood, (2000), 95, 6, 2098-2103, Brühl, J. Immunol., (2001), 166, 2420-2426. A particularly preferred molecular format of the invention provides a polypeptide construct wherein the CD3 specific binding domain of the construct of the invention comprises at least one V_H and one V_L region as defined above. It is of note that in addition to a V_H-region as defined herein and having reduced propensity to generate T cell epitopes, said specific binding construct may comprise additional

regions/domains with reduced propensity to generate T cell epitopes. As mentioned above, also the VL-region and/or the corresponding frameworks may comprise amino acid stretches which have been engineered in accordance with this invention to having reduced propensity for T cell epitope generation. The intramolecular orientation of the V_H-domain and the V_L-domain, which are linked to each other by a linker-domain, in the scFv format is not decisive for the recited bispecific single chain constructs. Thus, scFvs with both possible arrangements (V_H-domain – linker domain – V_L-domain; V_L-domain – linker domain – V_H-domain) are particular embodiments of the recited bispecific single chain construct. A CD3 specific domain can be located N- or C-terminally in the bispecific molecule. VH and VL regions of each domain can be arranged in different orders (V_H-V_L or V_L-V_H).

The term "single-chain" as used in accordance with the present invention means that said first and second domain of the bispecific single chain construct are covalently linked, preferably in the form of a co-linear amino acid sequence encoded by a single nucleic acid molecule.

It is of note that the construct of the invention may comprise, in addition to the herein defined first domain and the Ig-derived second domain (an) additional domain(s), e.g. for the isolation and/or preparation of recombinantly produced constructs.

It is of note that, in accordance with this invention, not only the above described first domain which specifically binds to human CD3 of the inventive CD3 construct may have reduced propensity to generate T cell epitopes. It is also envisaged that the Ig-derived second domain and/or (a) connecting linker-region(s) is (are) modified, for example humanized and/or also deimmunized.

As mentioned above, deimmunization approaches are in particular illustrated in WO 92/10755, WO 00/34317, WO 98/52976, WO 02/079415 or WO 02/012899 and the appended examples. These approaches entail carrying out substitutions of amino acids within potential T cell epitopes. In this way, the likelihood that a given sequence will give rise to T cell epitopes upon intracellular protein processing is reduced.

Furthermore, "humanization approaches" are well known in the art and in particular described for antibody molecules, e.g. Ig-derived molecules. The term "humanized" refers to humanized forms of non-human (e.g., murine) antibodies or fragments thereof (such as Fv, Fab, Fab', F(ab'), scFvs, or other antigen-binding partial sequences of antibodies) which contain some portion of the sequence derived from non-human antibody. Humanized antibodies include human immunoglobulins in which residues from a complementary determining region (CDR) of the human immunoglobulin are replaced by residues from a CDR of a non-human species such as mouse, rat or rabbit having the desired binding specificity, affinity and capacity. In general, the humanized antibody will comprise substantially all of at least one, and generally two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin ; see, inter alia, Jones et al., *Nature* 321:522-525 (1986), Presta, *Curr. Op. Struct. Biol. 2:593-596* (1992). Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acids introduced into it from a source which is non-human in order to more closely resemble a human antibody, while still retaining the original binding activity of the antibody. Methods for humanization of antibodies/antibody molecules are further detailed in Jones et al., *Nature* 321:522-525 (1986); Riechmann et al., *Nature* 332:323-327 (1988); and Verhoeyen et al., *Science* 239:1534-1536 (1988). Specific examples of humanized antibodies, e.g. antibodies directed against EpCAM , are known in the art, see e.g. (LoBuglio, Proceedings of the American Society of Clinical Oncology (Abstract). 1997, 1562 and Khor, Proceedings of the American Society of Clinical Oncology (Abstract), 1997, 847).

Accordingly, in the context of this invention, in particular bispecific single chain antibody constructs are provided, which are deimmunized and can successfully be employed in pharmaceutical compositions.

As mentioned above, the Ig-derived second domain of the above-described CD3 specific binding construct may comprise an antigen-interaction-site with specificity for

a cell surface molecule.

The term "cell surface molecule", as used herein, also denotes molecules which are presented on the surface of cells. The term "cell surface molecule", relates to molecules, which are presented on the surface of cells and comprise domains or epitopes accessible (in vitro or in vivo) to Ig-derived binding domains, preferably antibodies, antibody fragments or derivatives. As illustrated above, most preferably said Ig-derived domain is a scFv. Examples for said cell surface molecules are membrane and transmembrane proteins, molecules adapted to said proteins or the cell surface etc. According to a further preferred embodiment of the invention said cell surface molecule is a tumor specific marker. In context of this invention, the term "tumor specific marker" relate to molecules, which are presented and/or located on the surface of tumor cells or which are ubiquitously expressed but are only accessible for binding of antibodies, antibody fragments or antibody derivatives on the surface of tumor cells. Examples of tumor markers are given herein below and comprise, but are not limited to, EpCAM, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, $MUC5_{AC}$, $MUC5_{B}$, MUC7, Lewis-Y, CD20, CD33, CD30, CD44v6, Wue-1, Plasma Cell Antigen (see WO 01/47953), (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), STEAP, mesothelin, Prostate Stem Cell Antigen (PSCA), sTn (sialylated Tn antigen), FAP (fibroblast activation antigen), EGFRvIII, Igα, Igβ, MT-MMPs, Cora antigen, EphA2, L6 and CO-29.

The Ig-derived second domain of the CD3 specific binding construct of the invention may also comprise an antigen-interaction site with a specificity for a molecule selected from the group consisting of EpCAM, CCR5, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, $MUC5_{AC}$, $MUC5_{B}$, MUC7, βhCG, Lewis-Y, CD20, CD33, CD30, ganglioside GD3, 9-O-Acetyl-GD3, GM2, Globo H, fucosyl GM1, Poly SA, GD2, Carboanhydrase IX (MN/CA IX), CD44v6, Sonic Hedgehog (Shh), Wue-1, Plasma Cell Antigen, (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), CCR8, TNF-alpha precursor, STEAP, mesothelin, A33 Antigen, Prostate Stem Cell Antigen (PSCA), Ly-6; desmoglein 4, E-cadherin neoepitope, Fetal Acetylcholine Receptor, CD25, CA19-9 marker, CA-125 marker and Muellerian Inhibitory Substance (MIS) Receptor type II, sTn (sialylated Tn antigen), FAP (fibroblast

activation antigen), endosialin, EGFRvIII, L6, SAS, CD63, TAG72, TF-antigen, Cora antigen, CD7, CD22, Igα (CD79a), Igβ (CD79b), G250, gp100, MT-MMPs, F19-antigen, CO-29 and EphA2.

The constructs provided herein are particular useful in medical setting. For example, tumorous diseases and/or lymphomas, preferably non-Hodgkin's B-cell lymphoma, may be treated with an inventive deimmunized (bispecific) construct directed against human CD3 and CD20 (CD3xCD20 or CD20xCD3). Autoimmune diseases may be treated by the administration of deimmunized (bispecific) constructs directed against human CD3 and CD30 or CD19 (i.e CD3xCD30 or CD30xCD3 or CD3xCD19 or CD19xCD3). Rheumatoid arthritis, as well as other inflammatory diseases may be treated with an inventive deimmunized (bispecific) construct directed against human CD3 and CCR5 (CD3xCCR5 or CCR5xCD3). A deimmunized CD3 specific binding construct as defined herein and comprising a second Ig-derived domain directed to/binding with TNF-alpha precursor may also be useful in the treatment or prevention of inflammatory disorders. CD3 constructs as provided herein and comprising a second, Ig-derived domain directed against/binding to/interacting with EpCAM, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, $MUC5_{AC}$, $MUC5_{B}$, MUC7, Lewis-Y, CD20, CD33, CD30, CD44v6, Wue-1, Plasma Cell Antigen (see WO 01/47953), (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), STEAP, mesothelin, Prostate Stem Cell Antigen (PSCA), sTn (sialylated Tn antigen), FAP (fibroblast activation antigen), EGFRvIII, Igα, Igβ, MT-MMPs, Cora antigen, EphA2, L6 and CO-29 may be particularly useful in the medical intervention of tumorous diseases like breast cancer, colon cancer, prostate cancer, head and neck cancer, skin cancer (melanoma), cancers of the genito-urinary tract, e.g. ovarial cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer, cancers of the bile duct, esophagus cancer, cancer of the salivatory glands and cancer of the thyroid gland or other tumorous diseases like hematological tumors, gliomas, sarcomas or osteosarcomas. The administration of the CD3 binding constructs is also indicated for minimal residual disease, preferably for early solid tumors, advanced solid tumors or metastatic solid tumors.

As also illustrated in the appended examples, a particularly preferred CD3 specific binding construct of the invention comprises the above defined first domain with reduced propensity to generate T cell epitopes and a second, Ig-derived domain comprising an antigen-interaction site with a specificity for EpCAM.

Epithelial cell adhesion molecule (EpCAM, also called 17-1A antigen, KSA, EGP40, GA733-2, ks1-4 or esa) is a 40-kDa membrane-integrated glycoprotein of 314 amino acids with specific expression in certain epithelia and on many human carcinomas (reviewed in Balzar, J. Mol. Med. 1999, 77, 699-712). EpCAM was discovered and subsequently cloned through its recognition by the murine monoclonal antibody 17-1A/edrecolomab (Goettlinger, Int J Cancer. 1986; 38, 47-53 and Simon, Proc. Natl. Acad. Sci. USA. 1990; 87, 2755-2759). EpCAM serves to adhere epithelial cells in an oriented and highly ordered fashion (Litvinov, J Cell Biol. 1997, 139, 1337-1348). Upon malignant transformation of epithelial cells the rapidly growing tumor cells are abandoning the high cellular order of epithelia. Consequently, the surface distribution of EpCAM becomes less restricted and the molecule better exposed on tumor cells and accessible for binding of antibodies, antibody fragments or antibody derivatives on the surface of tumor cells. Due to their epithelial cell origin, tumor cells from most carcinomas still express EpCAM on their surface.

In vivo, expression of EpCAM is related to increased epithelial proliferation and negatively correlates with cell differentiation (for review see Balzar, 1999, J. Mol. Med. 77, 699-712). Expression of EpCAM is essentially seen with all major carcinomas (reviewed in Balzar, J Mol Med. 1999, 77, 699-712 or documented, inter alia, in De Bree, Nucl Med Commun. 1994, 15, 613-27; Zhang, Clin Cancer Res. 1998, 4, 295-302). Because of its widespread expression, EpCAM is referred to as a "pan-carcinoma" antigen. In many cases, tumor cells were observed to express EpCAM to a much higher degree than their parental epithelium or less aggressive forms of said cancers. For example, increased EpCAM expression represents an early event in the development of prostate cancer (Poczatek, J Urol., 1999, 162, 1462-1644). In addition, in the majority of both squamous and adenocarcinomas of the cervix a strong EpCAM expression correlates with an increased proliferation and the disappearance of markers for terminal differentiation (Litvinov, Am. J. Pathol. 1996, 148, 865-75). In breast cancer, overexpression of EpCAM on tumor cells is a

predictor of survival (Gastl, Lancet. 2000, 356, 1981-1982). EpCAM is a marker for the detection of disseminated tumor cells in patients suffering from squamous cell carcinoma of the head, neck and lung (Chaubal, Anticancer Res 1999, 19, 2237-2242, Piyathilake, Hum Pathol. 2000, 31, 482-487). Normal squamous epithelium, as found in epidermis, oral cavity, epiglottis, pharynx, larynx and esophagus did not significantly express EpCAM (Quak, Hybridoma, 1990, 9, 377-387). EpCAM has been shown to be expressed on the majority of primary, metastatic, and disseminated NSCLC (non small cell lung cancer cells (Passlick, Int J Cancer, 2000, 87, 548-552)), on gastric and gastro-oesophageal junction adenocarcinomas (Martin, J Clin Pathol 1999, 52, 701-4) and in cell lines derived from colorectal, pancreatic carcinomas and breast carcinomas (Szala, Proc Natl Acad Sci U S A 1990, 87, 3542-6, Packeisen, Hybridoma, 1999, 18, 37-40).

In a most preferred embodiment, the CD3 specific binding construct of the invention which comprises a second Ig-derived domain directed against/binding to EpCAM, comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b).

Accordingly, the present invention provides, in a particularly preferred embodiment for specific CD3 constructs which comprise a CD3 binding/interaction part ("anti-CD3") which has reduced propensity to generate T cell epitopes and a further single chain part (an Ig-derived domain) which specifically interacts with/binds to EpCAM ("anti-EpCAM"). The following tables 1A, 1B, 2A, 2B, 3A, 3B, 4A, 4B, 5A and 5B relate to preferred configurations of such CD3 and EpCAM binding constructs.

EpCAM 3-1, EpCAM 3-5, EpCAM 4-1, EpCAM 4-7 and EpCAM 5-10 relate to specific single chain antibodies against EpCAM isolated by phage display in WO99/25818.

Each protein construct in Tables 1A, 2A, 3A, 4A and 5A comprises 7 distinct protein modules, denoted A-G. Protein modules A-G are directly and covalently linked to one another in a single contiguous polypeptide chain by peptide bonds in the order A-B-C-D-E-F-G, with protein module A at the N-terminus and protein module G at the C-terminus. Protein modules A, C, E and G denote antibody variable domains which can be either VH or VL domains of antibodies having specificity for the human CD3 or EpCAM antigen. The modules B, D and F are linkers connecting the VH and VL domains.

If protein module A is a VH antibody domain, then protein module C is a VL protein domain, and vice versa. If protein module E is a VH antibody domain, then protein module G is a VL protein domain, and vice versa.

Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 78, 80 or 82. The VH protein domain of human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO: 137, 141, 145, 149 and 133, respectively. The VL protein domain of human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO: 139, 143, 147, 151 and 135, respectively.

Pairs of antibody variable domains denoted by the protein module pairs A/C and E/G are joined by additional linking protein modules, wherein protein module B serves to directly link the module pair A/C and protein module F serves to directly link the module pair E/G. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the EpCAM antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 168. The module D connects the ABC and EFG module groups.

The combination of protein modules A-B-C and the combination of protein modules E-F-G each respectively constitute one scFv fragment of an antibody having

specificity for either the human CD3 antigen or for the EpCAM antigen. If the modules A and C show the CD3 binding sequence, the respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 176. On the other hand, if the modules A and C show the EpCAM binding sequence, the respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 174. Thus, an additional serine may be inserted after the VL chain for cloning purposes. However, the skilled artisan may also use the linker as shown in SEQ ID NO.:174 in order to link a VL domain with the subsequent V domain instead of SEQ ID NO.:176. Protein module D serves to connect the C-terminal end of protein module C with the N-terminal end of protein module E.

Each nucleic acid construct in Tables 1B, 2B, 3B, 4B and 5B comprises 7 distinct nucleic acid modules, denoted A-G. Nucleic acid modules A-G are directly and covalently linked to one another in a single contiguous nucleotide chain by phosphate glycoside bonds in the order A-B-C-D-E-F-G, with nucleic acid module A at the 5'-end and nucleic acid module G at the 3'-end of a respective nucleic acid construct. Nucleic acid modules A, C, E and G denote encoding regions for antibody variable domains which can be either VH or VL domains of antibodies having specificity for the human CD3 or EpCAM antigen.

If nucleic acid module A encodes a VH antibody domain, then nucleic acid module C encodes a VL protein domain, and vice versa. If nucleic acid module E encodes a VH antibody domain, then nucleic acid module G encodes a VL protein domain, and vice versa.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 77, 79 or 81. The nucleic acid molecule encoding the VH protein domain of the human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO: 136,140, 144, 148 and 132

respectively. The nucleic acid molecule encoding the VL protein domain of the human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO: 138,142, 146, 150 and 134, respectively.

Pairs of nucleic acids encoding antibody variable domains denoted by the nucleic acid module pairs A/C and E/G are joined by additional linking nucleic acid modules, wherein nucleic acid module B serves to directly link the module pair A/C and nucleic acid module F serves to directly link the module pair E/G. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the nucleotide sequence as set out in SEQ ID NO: 202. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the human EpCAM antigen, nucleic acid module B or F, respectively, has the nucleotide sequence as set out in SEQ ID NO: 201.

The combination of nucleic acid modules A-B-C and the combination of nucleic acid modules E-F-G each respectively constitute one scFv fragment of an antibody having specificity for either the human CD3 antigen or for the EpCAM antigen. If the A and C modules comprise CD3 binding sequences, the respective groups of nucleic acid modules A-B-C and E-F-G are connected to each other through nucleic acid module D, having the nucleotide sequence as set out in SEQ ID NO: 175. If the A and C modules comprise EpCAM binding sequences, the respective groups of nucleic acid modules A-B-C and E-F-G are connected to each other through nucleic acid module D, having the nucleotide sequence as set out in SEQ ID NO: 173. However, as mentioned above, the additional codon encoding a serine (in SEQ ID NO.:175) may be inserted for cloning purposes. The skilled person may link the nucleotide sequence encoding the VL chain directly with the subsequent V domain with the linker as depicted in SEQ ID NO.:173 without the additional codon encoding serine at the 5' end of the linker. Nucleic acid module D serves to connect the 3'-end of nucleic acid module C with the 5'-end of nucleic acid module E.

Table 1A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-1 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion …							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	137	168	139	CD3 (VL2/ VH5)xEPCAM(3-1)	LHHL
2	74	3	80	176	137	168	139	CD3 (VH5/VL2)xEPCAM(3-1)	HLHL
3	80	3	74	176	139	168	137	CD3 (VL2/ VH5)xEPCAM(3-1)	LHLH
4	74	3	80	176	139	168	137	CD3 (VH5/VL2)xEPCAM(3-1)	HLLH
5	139	168	137	174	74	3	80	EPCAM(3-1)xCD3 (VH5/VL2)	LHHL
6	137	168	139	174	74	3	80	EPCAM(3-1)xCD3(VH5/VL2)	HLHL
7	139	168	137	174	80	3	74	EPCAM(3-1)xCD3 (VL2/ VH5)	LHLH
8	137	168	139	174	80	3	74	EPCAM(3-1)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	137	168	139	CD3 (VL2/ VH7)xEPCAM(3-1)	LHHL
10	76	3	80	176	137	168	139	CD3 (VH7/VL2)xEPCAM(3-1)	HLHL
11	80	3	76	176	139	168	137	CD3 (VL2/VH7)xEPCAM(3-1)	LHLH
12	76	3	80	176	139	168	137	CD3 (VH7/VL2)xEPCAM(3-1)	HLLH
13	139	168	137	174	76	3	80	EPCAM(3-1)xCD3 (VH7/VL2)	LHHL
14	137	168	139	174	76	3	80	EPCAM(3-1)xCD3(VH7/VL2)	HLHL
15	139	168	137	174	80	3	76	EPCAM(3-1)xCD3 (VL2/ VH7)	LHLH
16	137	168	139	174	80	3	76	EPCAM(3-1)xCD3(VL2/ VH7)	HLLH

Table 1B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-1 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	136	201	138	CD3 (VL2/ VH5)xEPCAM(3-1)	LHHL
2	73	202	79	175	136	201	138	CD3 (VH5/VL2)xEPCAM(3-1)	HLHL
3	79	202	73	175	138	201	136	CD3 (VL2/ VH5)xEPCAM(3-1)	LHLH
4	73	202	79	175	138	201	136	CD3 (VH5/VL2)xEPCAM(3-1)	HLLH
5	138	201	136	173	73	202	79	EPCAM(3-1)xCD3 (VH5/VL2)	LHHL
6	136	201	138	173	73	202	79	EPCAM(3-1)xCD3(VH5/VL2)	HLHL
7	138	201	136	173	79	202	73	EPCAM(3-1)xCD3 (VL2/ VH5)	LHLH
8	136	201	138	173	79	202	73	EPCAM(3-1)xCD3(VL2/ VH5)	HLLH
9	79	202	75	175	136	201	138	CD3 (VL2/ VH7)xEPCAM(3-1)	LHHL
10	75	202	79	175	136	201	138	CD3 (VH7/VL2)xEPCAM(3-1)	HLHL
11	79	202	75	175	138	201	136	CD3 (VL2/ VH7)xEPCAM(3-1)	LHLH
12	75	202	79	175	138	201	136	CD3 (VH7/VL2)xEPCAM(3-1)	HLLH
13	138	201	136	173	75	202	79	EPCAM(3-1)xCD3 (VH7/VL2)	LHHL
14	136	201	138	173	75	202	79	EPCAM(3-1)xCD3(VH7/VL2)	HLHL
15	138	201	136	173	79	202	75	EPCAM(3-1)xCD3 (VL2/ VH7)	LHLH
16	136	201	138	173	79	202	75	EPCAM(3-1)xCD3(VL2/ VH7)	HLLH

Table 2A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-5 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion …							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	141	168	143	CD3 (VL2/VH5)xEPCAM(3-5)	LHHL
2	74	3	80	176	141	168	143	CD3 (VH5/VL2)xEPCAM(3-5)	HLHL
3	80	3	74	176	143	168	141	CD3 (VL2/VH5)xEPCAM(3-5)	LHLH
4	74	3	80	176	143	168	141	CD3 (VH5/VL2)xEPCAM(3-5)	HLLH
5	143	168	141	174	74	3	80	EPCAM(3-5)xCD3 (VH5/VL2)	LHHL
6	141	168	143	174	74	3	80	EPCAM(3-5)xCD3(VH5/VL2)	HLHL
7	143	168	141	174	80	3	74	EPCAM(3-5)xCD3 (VL2/VH5)	LHLH
8	141	168	143	174	80	3	74	EPCAM(3-5)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	141	168	143	CD3 (VL2/VH7)xEPCAM(35)	LHHL
10	76	3	80	176	141	168	143	CD3 (VH7/VL2)xEPCAM(3-5)	HLHL
11	80	3	76	176	143	168	141	CD3 (VL2/VH7)xEPCAM(3-5)	LHLH
12	76	3	80	176	143	168	141	CD3 (VH7/VL2)xEPCAM(3-5)	HLLH
13	143	168	141	174	76	3	80	EPCAM(3-5)xCD3 (VH7/VL2)	LHHL
14	141	168	143	174	76	3	80	EPCAM(3-5)xCD3(VH7/VL2)	HLHL
15	143	168	141	174	80	3	76	EPCAM(3-5)xCD3 (VL2/VH7)	LHLH
16	141	168	143	174	80	3	76	EPCAM(3-5)xCD3(VL2/ VH7)	HLLH

Table 2B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-5 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	140	201	142	CD3 (VL2/ VH5)xEPCAM(3-5)	LHHL
2	73	202	79	175	140	201	142	CD3 (VH5/VL2)xEPCAM(3-5)	HLHL
3	79	202	73	175	142	201	140	CD3 (VL2/ VH5)xEPCAM(3-5)	LHLH
4	73	202	79	175	142	201	140	CD3 (VH5/VL2)xEPCAM(3-5)	HLLH
5	142	201	140	173	73	202	79	EPCAM(3-5)xCD3(VH5/VL2)	LHHL
6	140	201	142	173	73	202	79	EPCAM(3-5)xCD3(VH5/VL2)	HLHL
7	142	201	140	173	79	202	73	EPCAM(3-5)xCD3 (VL2/VH5)	LHLH
8	140	201	142	173	79	202	73	EPCAM(3-5)xCD3(VL2/VH5)	HLLH
9	79	202	75	175	140	201	142	CD3 (VL2/ VH7)xEPCAM(3-5)	LHHL
10	75	202	79	175	140	201	142	CD3 (VH7/VL2)xEPCAM(3-5)	HLHL
11	79	202	75	175	142	201	140	CD3 (VL2/ VH7)xEPCAM(3-5)	LHLH
12	75	202	79	175	142	201	140	CD3 (VH7/VL2)xEPCAM(3-5)	HLLH
13	142	201	140	173	75	202	79	EPCAM(3-5)xCD3 (VH7/VL2)	LHHL
14	140	201	142	173	75	202	79	EPCAM(3-5)xCD3(VH7/VL2)	HLHL
15	142	201	140	173	79	202	75	EPCAM(3-5)xCD3 (VL2/VH7)	LHLH
16	140	201	142	173	79	202	75	EPCAM(3-5)xCD3(VL2/VH7)	HLLH

Table 3A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-1 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	145	168	147	CD3 (VL2/ VH5)xEPCAM(4-1)	LHHL
2	74	3	80	176	145	168	147	CD3 (VH5/VL2)xEPCAM(4-1)	HLHL
3	80	3	74	176	147	168	145	CD3 (VL2/ VH5)xEPCAM(4-1)	LHLH
4	74	3	80	176	147	168	145	CD3 (VH5/VL2)xEPCAM(4-1)	HLLH
5	147	168	145	174	74	3	80	EPCAM(4-1)xCD3 (VH5/VL2)	LHHL
6	145	168	147	174	74	3	80	EPCAM(4-1)xCD3(VH5/VL2)	HLHL
7	147	168	145	174	80	3	74	EPCAM(4-1)xCD3 (VL2/ VH5)	LHLH
8	145	168	147	174	80	3	74	EPCAM(4-1)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	145	168	147	CD3 (VL2/ VH7)xEPCAM(4-1)	LHHL
10	76	3	80	176	145	168	147	CD3 (VH7/VL2)xEPCAM(4-1)	HLHL
11	80	3	76	176	147	168	145	CD3 (VL2/ VH7)xEPCAM(4-1)	LHLH
12	76	3	80	176	147	168	145	CD3 (VH7/VL2)xEPCAM(4-1)	HLLH
13	147	168	145	174	76	3	80	EPCAM(4-1)xCD3 (VH7/VL2)	LHHL
14	145	168	147	174	76	3	80	EPCAM(4-1)xCD3(VH7/VL2)	HLHL
15	147	168	145	174	80	3	76	EPCAM(4-1)xCD3 (VL2/ VH7)	LHLH
16	145	168	147	174	80	3	76	EPCAM(4-1)xCD3(VL2/ VH7)	HLLH

Table 3B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-1 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	144	201	146	CD3 (VL2/ VH5)xEPCAM(4-1)	LHHL
2	73	202	79	175	144	201	146	CD3 (VH5/VL2)xEPCAM(4-1)	HLHL
3	79	202	73	175	146	201	144	CD3 (VL2/ VH5)xEPCAM(4-1)	LHLH
4	73	202	79	175	146	201	144	CD3 (VH5/VL2)xEPCAM(4-1)	HLLH
5	146	201	144	173	73	202	79	EPCAM(4-1)xCD3 (VH5/VL2)	LHHL
6	144	201	146	173	73	202	79	EPCAM(4-1)xCD3(VH5/VL2)	HLHL
7	146	201	144	173	79	202	73	EPCAM(4-1)xCD3 (VL2/ VH5)	LHLH
8	144	201	146	173	79	202	73	EPCAM(4-1)xCD3(VL2/ VH5)	HLLH
9	79	202	75	175	144	201	146	CD3 (VL2/ VH7)xEPCAM(4-1)	LHHL
10	75	202	79	175	144	201	146	CD3 (VH7/VL2)xEPCAM(4-1)	HLHL
11	79	202	75	175	146	201	144	CD3 (VL2/ VH7)xEPCAM(4-1)	LHLH
12	75	202	79	175	146	201	144	CD3 (VH7/VL2)xEPCAM(4-1)	HLLH
13	146	201	144	173	75	202	79	EPCAM(4-1)xCD3 (VH7/VL2)	LHHL
14	144	201	146	173	75	202	79	EPCAM(4-1)xCD3(VH7/VL2)	HLHL
15	146	201	144	173	79	202	75	EPCAM(4-1)xCD3 (VL2/ VH7)	LHLH
16	144	201	146	173	79	202	75	EPCAM(4-1)xCD3(VL2/ VH7)	HLLH

Table 4A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-7 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	149	168	151	CD3 (VL2/ VH5)xEPCAM(4-7)	LHHL
2	74	3	80	176	149	168	151	CD3 (VH5/VL2)xEPCAM(4-7)	HLHL
3	80	3	74	176	151	168	149	CD3 (VL2/ VH5)xEPCAM(4-7)	LHLH
4	74	3	80	176	151	168	149	CD3 (VH5/VL2)xEPCAM(4-7)	HLLH
5	151	168	149	174	74	3	80	EPCAM(4-7)xCD3 (VH5/VL2)	LHHL
6	149	168	151	174	74	3	80	EPCAM(4-7)xCD3(VH5/VL2)	HLHL
7	151	168	149	174	80	3	74	EPCAM(4-7)xCD3 (VL2/ VH5)	LHLH
8	149	168	151	174	80	3	74	EPCAM(4-7)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	149	168	151	CD3 (VL2/ VH7)xEPCAM(4-7)	LHHL
10	76	3	80	176	149	168	151	CD3 (VH7/VL2)xEPCAM(4-7)	HLHL
11	80	3	76	176	151	168	149	CD3 (VL2/ VH7)xEPCAM(4-7)	LHLH
12	76	3	80	176	151	168	149	CD3 (VH7/VL2)xEPCAM(4-7)	HLLH
13	151	168	149	174	76	3	80	EPCAM(4-7)xCD3 (VH7/VL2)	LHHL
14	149	168	151	174	76	3	80	EPCAM(4-7)xCD3(VH7/VL2)	HLHL
15	151	168	149	174	80	3	76	EPCAM(4-7)xCD3 (VL2/ VH7)	LHLH
16	149	168	151	174	80	3	76	EPCAM(4-7)xCD3(VL2/ VH7)	HLLH

Table 4B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-7 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	148	201	150	CD3 (VL2/ VH5)xEPCAM(4-7)	LHHL
2	73	202	79	175	148	201	150	CD3 (VH5/VL2)xEPCAM(4-7)	HLHL
3	79	202	73	175	150	201	148	CD3 (VL2/ VH5)xEPCAM(4-7)	LHLH
4	73	202	79	175	150	201	148	CD3 (VH5/VL2)xEPCAM(4-7)	HLLH
5	150	201	148	173	73	202	79	EPCAM(4-7)xCD3 (VH5/VL2)	LHHL
6	148	201	150	173	73	202	79	EPCAM(4-7)xCD3(VH5/VL2)	HLHL
7	150	201	148	173	79	202	73	EPCAM(4-7)xCD3 (VL2/ VH5)	LHLH
8	148	201	150	173	79	202	73	EPCAM(4-7)xCD3(VL2/ VH5)	HLLH
9	79	202	75	175	148	201	150	CD3 (VL2/ VH7)xEPCAM(4-7)	LHHL
10	75	202	79	175	148	201	150	CD3 (VH7/VL2)xEPCAM(4-7)	HLHL
11	79	202	75	175	150	201	148	CD3 (VL2/ VH7)xEPCAM(4-7)	LHLH
12	75	202	79	175	150	201	148	CD3 (VH7/VL2)xEPCAM(4-7)	HLLH
13	150	201	148	173	75	202	79	EPCAM(4-7)xCD3 (VH7/VL2)	LHHL
14	148	201	150	173	75	202	79	EPCAM(4-7)xCD3(VH7/VL2)	HLHL
15	150	201	148	173	79	202	75	EPCAM(4-7)xCD3 (VL2/ VH7)	LHLH
16	148	201	150	173	79	202	75	EPCAM(4-7)xCD3(VL2/ VH7)	HLLH

Table 5A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 5-10 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	133	168	135	CD3 (VL2/ VH5)xEPCAM(5-10)	LHHL
2	74	3	80	176	133	168	135	CD3 (VH5/VL2)xEPCAM(5-10)	HLHL
3	80	3	74	176	135	168	133	CD3 (VL2/ VH5)xEPCAM(5-10)	LHLH
4	74	3	80	176	135	168	133	CD3 (VH5/VL2)xEPCAM(5-10)	HLLH
5	135	168	133	174	74	3	80	EPCAM(5-10)xCD3 (VH5/VL2)	LHHL
6	133	168	135	174	74	3	80	EPCAM(5-10)xCD3(VH5/VL2)	HLHL
7	135	168	133	174	80	3	74	EPCAM(5-10)xCD3 (VL2/ VH5)	LHLH
8	133	168	135	174	80	3	74	EPCAM(5-10)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	133	168	135	CD3(VL2/ VH7) xEPCAM(5-10)	LHHL
10	76	3	80	176	133	168	135	CD3 (VH7/VL2) xEPCAM(5-10)	HLHL
11	80	3	76	176	135	168	133	CD3(VL2/VH7) xEPCAM(5-10)	LHLH
12	76	3	80	176	135	168	133	CD3 (VH7/VL2) xEPCAM(5-10)	HLLH
13	135	168	133	174	76	3	80	EPCAM(5-10)xCD3 (VH7/VL2)	LHHL
14	133	168	135	174	76	3	80	EPCAM(5-10)xCD3(VH7/VL2)	HLHL
15	135	168	133	174	80	3	76	EPCAM(5-10)xCD3 (VL2/ VH7)	LHLH
16	133	168	135	174	80	3	76	EPCAM(5-10)xCD3(VL2/ VH7)	HLLH

Table 5B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 5-10 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	132	201	134	CD3 (VL2/ VH5) xEPCAM(5-10)	LHHL
2	73	202	79	175	132	201	134	CD3 (VH5/VL2) xEPCAM(5-10)	HLHL
3	79	202	73	175	134	201	132	CD3 (VL2/ VH5) xEPCAM(5-10)	LHLH
4	73	202	79	175	134	201	132	CD3 (VH5/VL2) xEPCAM(5-10)	HLLH
5	134	201	132	173	73	202	79	EPCAM(5-10)xCD3 (VH5/VL2)	LHHL
6	132	201	134	173	73	202	79	EPCAM(5-10)xCD3(VH5/VL2)	HLHL
7	134	201	132	173	79	202	73	EPCAM(5-10)xCD3 (VL2/ VH5)	LHLH
8	132	201	134	173	79	202	73	EPCAM(5-10)xCD3(VL2/ VH5)	HLLH
9	79	202	75	175	132	201	134	CD3 (VL2/ VH7) xEPCAM(5-10)	LHHL
10	75	202	79	175	132	201	134	CD3 (VH7/VL2) xEPCAM(5-10)	HLHL
11	79	202	75	175	134	201	132	CD3 (VL2/ VH7) xEPCAM(5-10)	LHLH
12	75	202	79	175	134	201	132	CD3 (VH7/VL2) xEPCAM(5-10)	HLLH
13	134	201	132	173	75	202	79	EPCAM(5-10)xCD3 (VH7/VL2)	LHHL
14	132	201	134	173	75	202	79	EPCAM(5-10)xCD3(VH7/VL2)	HLHL
15	134	201	132	173	79	202	75	EPCAM(5-10)xCD3 (VL2/ VH7)	LHLH
16	132	201	134	173	79	202	75	EPCAM(5-10)xCD3(VL2/ VH7)	HLLH

Most preferably, the invention provides bispecific antibody constructs comprising a specificity binding to CD3 and EpCAM and having the SEQ ID NO.:30, 31 (construct 2 of Table 1A and 1B), Seq ID NO.: 48, 49 (construct 5 of the Table 1A, 1B), SEQ ID NO.: 64, 65 (construct 2 of Table 2A, 2B), SEQ ID NO: 54, 55 (construct 5 of Table 2A, 2B), Seq ID NO.: 66, 67 (construct 2 of Table 3A, 3B), SEQ ID NO.: 32, 33 (construct 2 of Table 4A, 4B), SEQ ID NO.:34, 35 (construct 4 of Table 4A, 4B), SEQ ID NO.: 60, 61 (construct 5 of Table 4A, 4B), SEQ ID NO.: 36, 37 (construct 2 of Table 5A, 5B), SEQ ID NO.: 38, 39 (construct 4 of Table 5A, 5B) or SEQ ID NO.:62, 63 (construct 5 of Table 5A, 5B).

In accordance with constructs provided herein above, particularly preferred CD3 and EpCAM binding constructs of the invention, comprising at least the above described first domain with reduced propensity for T cell epitope generation and specificity for human CD3 and a second, Ig-derived domain which is specific for EpCAM are shown in SEQ ID NOs.: 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325. Corresponding nucleic acid molecules encoding said preferred CD3 and EpCAM binding constructs as defined herein comprise SEQ ID NOs: 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324.

Accordingly, the present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to EpCAM, selected from the group consisting of

(a) an amino acid sequence as shown in any one of SEQ ID NO 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257,.259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299; 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 or 325;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 or 324;

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridization conditions;

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to EpCAM, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NO 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 or 324 under stringent hybridization conditions.

The term "hybridizing" as used herein refers to polynucleotides/nucleic acid sequences which are capable of hybridizing to the polynucleotides encoding the deimmunized constructs as defined herein. Therefore, said polynucleotides may be useful as probes in Northern or Southern Blot analysis of RNA or DNA preparations, respectively, or can be used as oligonucleotide primers in PCR analysis dependent on their respective size. Preferably, said hybridizing polynucleotides comprise at least 10, more preferably at least 15 nucleotides in length while a hybridizing polynucleotide of the present invention to be used as a probe preferably comprises at least 100, more preferably at least 200, or most preferably at least 500 nucleotides in length.

It is well known in the art how to perform hybridization experiments with nucleic acid molecules, i.e. the person skilled in the art knows what hybridization conditions s/he has to use in accordance with the present invention. Such hybridization conditions

are referred to in standard text books such as Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory (2001) N.Y. Preferred in accordance with the present inventions are polynucleotides which are capable of hybridizing to the polynucleotides of the invention or parts thereof, under stringent hybridization conditions.

"Stringent hybridization conditions" refer, i.e. to an overnight incubation at 42°C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1 x SSC at about 65°C. Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH_2PO_4; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 µg/ml salmon sperm blocking DNA; followed by washes at 50°C with 1 X SSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC). It is of note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

The recited nucleic acid molecules may be, e.g., DNA, cDNA, RNA or synthetically produced DNA or RNA or a recombinantly produced chimeric nucleic acid molecule comprising any of those polynucleotides either alone or in combination.

The deimmunized CD3 and EpCAM binding constructs provided in this invention are particularly useful in medical settings, for example in the prevention, treatment and/or the amelioration of tumorous diseases, in particular, breast cancer, colon cancer, prostate cancer, head and neck cancer, skin cancer (melanoma), cancers of the

genito-urinary tract, e.g. ovarial cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer, cancers of the bile duct, esophagus cancer, cancer of the salivatory glands and cancer of the thyroid gland. In particular, the deimmunized constructs binding CD3 and EpCAM can be used for the treatment of epithelial cancer, preferably adenocarcinomas, or minimal residual disease, more preferably early solid tumor, advanced solid tumor or metastatic solid tumor.

In a more particularly preferred embodiment of the CD3 specific binding construct described herein, said construct comprises a second Ig-derived domain which comprises an antigen-interaction site with a specificity CCR5.
The chemokine receptor CCR5 is a member of a large family of G protein coupled seven transmembrane domain receptors that binds the proinflammatory chemokines RANTES, MIP1-α, MIP1-ß and MCP-2. Chemokines act in concert with adhesion molecules to induce the extravasation of leukocytes and to direct their migration to sites of tissue injury. CCR5 is expressed on a minority of T-cells and monocytes and is further the major co-receptor for M-trophic HIV-1 strains that predominate early in the course of an HIV-infection.
Human immunodeficiency virus (HIV) cannot enter human cells unless it first binds to two key molecules on the cell surface, CD4 and a co-receptor. The co-receptor that is initially recognized is CCR5, later in the life cycle of the virus another chemokine receptor CXCR4 becomes the co-receptor for HIV-1 (D'Souza, Nature Med. 2, 1293 (1996); Premack, Nature Med. 2, 1174; Fauci, Nature 384, 529 (1996)). The HIV-1 strains that cause most transmissions of viruses by sexual contact are called M-tropic viruses. These HIV-1 strains (also known as non-syncytia inducing (NSI) primary viruses) can replicate in primary CD4+ T-cells and macrophages and use the chemokine receptor CCR5 (and, less often, CCR3) as their coreceptor. The T-tropic viruses (sometimes called syncytia inducing (SI) primary visuses) can also replicate in primary CD4+ T-cells but can in addition infect established CD4+ T-cell lines in vitro, which they do via the chemokine receptor CXCR4 (fusin). Many of these T-tropic strains can use CCR5 in addition to CXCR4, and some can enter macrophages via CCR5, at least under certain in vitro conditions (D'Souza, Nature Med. 2, 1293 (1996); Premack, Nature Med. 2, 1174; Fauci, Nature 384, 529 (1996)). Whether other coreceptors contribute to HIV-1 pathogenesis is unresolved, but the

existence of another coreceptor for some T-tropic strains can be inferred from in vitro studies. Because M-tropic HIV-1 strains are implicated in about 90% of sexual transmissions of HIV, CCR5 is the predominant coreceptor for the virus in patients; transmission (or systemic establishment) of CXCR4-using (T-tropic) strains is rare (D'Souza, Nature Med. 2, 1293 (1996); Premack, Nature Med. 2, 1174; Fauci, Nature 384, 529 (1996), Paxton, Nature Med. 2, 412 (1996); Liu, Cell 86, 367 (1996); Samson, Nature 382, 722 (1996); Dean, Science 273, 1856 (1996); Huang, Nature Med. 2, 1240 (1996)). However, once SI viruses evolve in vivo (or if they are transmitted), they are especially virulent and cause faster disease progression (D'Souza, Nature Med. 2, 1293 (1996); Premack, Nature Med. 2, 1174; Fauci, Nature 384, 529 (1996), Schuitemaker, J. Virol. 66, 1354 (1992); Connor, J. Virol. 67, 1772 (1993); Richman, J. Infect. Dis. 169, 968 (1994); R. I. Connor et al., J. Exp. Med. 185, 621 (1997); Trkola, Nature 384, 184 (1996)).

The numbers and identity of coreceptor molecules on target cells, and the ability of HIV-1 strains to likely enter cells via the different coreceptors, seem to be critical determinants of disease progression. These factors are major influences on both host- and virus-dependent aspects of HIV-1 infection. For example, a homozygous defect (delta 32) in CCR5 correlates strongly with resistance to HIV-1 infection in vivo and in vitro. Individuals who are heterozygous for a defective CCR5 allele are at best weakly protected against infection and have only a modestly slowed disease progression (Paxton, Nature Med. 2, 412 (1996); Liu, Cell 86, 367 (1996); Samson, Nature 382, 722 (1996); Dean, Science 273, 1856 (1996); Huang et al., Nature Med. 2, 1240 (1996)). However, other factors can influence the level of CCR5 expression on activated CD4+ T-cells and thereby affect the efficiency of HIV-1 infection in vitro (Trkola, Nature 384, 184 (1996); Bleul, Proc. Natl. Acad. Sci. U.S.A. 94, 1925 (1997)).

For multiple sclerosis it was shown that CCR5 and CXCR3 are predominantly expressed on T-cells infiltrating demyelinating brain lesions, as well as in the peripheral blood of affected patients. Elimination of the T-cells would block the T-cell arm of this autoimmune disease.

High expression of CCR3 and CCR5 was also observed in T cells and B cells of lymph nodes derived from patients with Hodgkin's disease.

Diabetes type I is considered to be a T-cell mediated autoimmune disease. The expression of CCR5 receptor in the pancreas was associated with the progression of

type I diabetes in relevant animal models (Cameron (2000) J. Immunol. 165, 1102-1110). In particular, the CCR5 expression was associated with the development of insulinitis and spontaneous type I diabetes.

Several antibodies specifically binding to (human) CCR5 are known in the art and comprise, MC-1 (Mack (1998) J. Exp. Med. 187, 1215-1224 or MC-5 (Blanpain (2002) Mol Biol Cell. 13:723-37, Segerer (1999) Kidney Int. 56:52-64, Kraft (2001) J Biol Chem. 14;276:34408-18). The CCR-5 antibodies, in particular MC-1 and MC-5 may serve as a source for Ig-derived second domain of the CD3 specific construct of the invention. Accordingly, in a preferred embodiment, the invention relates to a bispecific construct comprising at least two domains, wherein the first domain provides for the specificity to human CD3 and has a reduced propensity to generate T cell epitopes and whereby said Ig-derived second domain is derived from an antibody specific for (human) CCR5. Most preferably, such a construct is a single chain scFV as defined herein .

MC-1 was shown to bind specifically to the first part of the second extracellular loop of human CCR5 and did not crossreact with CCR5 derived from rhesus macaques as shown in the appended examples. Therefore, it is preferred that the CD3 specific construct of this invention comprises, for example, VL and VH domains of an antibody (i.e. an Ig-derived second domain) specific for CCR5, preferably the human CCR5, and VH and VL domains of an antibody specific for the CD3 antigen. Said antibody specific for the human CCR5 is the murine anti-human CCR5 antibody MC-1, described, inter alia, in Mack (1998), J. Exp. Med. 187, 1215-1224 and in the appended examples. Yet, it is envisaged that other α-CCR5 antibodies, like MC-5 (as characterized in the appended examples and disclosed in Blanpain (2002) Mol Biol Cell. 13:723-37, Segerer (1999) Kidney Int. 56:52-64 and Kraft (2001) J Biol Chem. 14;276:34408-18 may be employed in the context of this invention.

In a particularly preferred embodiment of the present invention, CD3-specific binding constructs are provided, which comprise a deimmunized domain directed against/binding to/interacting with human CD3 and a second Ig-derived domain which specifically binds to/interacts with CCR5. Such constructs are shown in Table 6A and 6B. The modules A-G in Tables 6A and 6B can be defined as mentioned above for Tables 1-5. Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID

NOs: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 78, 80 or 82. The VH protein domain of human CCR5 antibody is as set out in SEQ ID NO: 129. The VL protein domain of human CCR5 antibody is as set out in SEQ ID NO: 131. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the EpCAM antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 168. The respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 174. However, as mentioned above an additional serine may be introduced for cloning purposes (linker as depicted in SEQ ID NO.:176) between the VL and subsequent V domain.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 77, 79 or 81. The nucleic acid molecule encoding the VH protein domain of the human CCR5 antibody is as set out in SEQ ID NO: 128. The nucleic acid molecule encoding the VL protein domain of the human CCR5 antibody is as set out in SEQ ID NO: 130. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO: 202. When either the module pair A/C or E/G denotes nucleic acid enconding a pair of VH/VL or VL/VH from an antibody having specificity for the CCR5 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO: 201. The groups of nucleic acid modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 173. An alternative linker SEQ ID NO.:175 may also be used to conjugate VL domain with a subsequent V domain (including an additional codon encoding a serine residue for cloning purposes).

Table 6A Deimmunized anti-human CD3 constructs comprising single chain anti-CCR5 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	174	129	168	131	CD3 (VL2/ VH5) xCCR5	LHHL
2	74	3	80	174	129	168	131	CD3 (VH5/VL2) xCCR5	HLHL
3	80	3	74	174	131	168	129	CD3 (VL2/ VH5) xCCR5	LHLH
4	74	3	80	174	131	168	129	CD3 (VH5/VL2) xCCR5	HLLH
5	131	168	129	174	74	3	80	CCR5xCD3 (VH5/VL2)	LHHL
6	129	168	131	174	74	3	80	CCR5xCD3(VH5/VL2)	HLHL
7	131	168	129	174	80	3	74	CCR5xCD3 (VL2/ VH5)	LHLH
8	129	168	131	174	80	3	74	CCR5xCD3(VL2/ VH5)	HLLH
9	80	3	76	174	129	168	131	CD3 (VL2/ VH7) xCCR5	LHHL
10	76	3	80	174	129	168	131	CD3 (VH7/VL2) xCCR5	HLHL
11	80	3	76	174	131	168	129	CD3 (VL2/ VH7) xCCR5	LHLH
12	76	3	80	174	131	168	129	CD3 (VH7/VL2) xCCR5	HLLH
13	131	168	129	174	76	3	80	CCR5xCD3 (VH7/VL2)	LHHL
14	129	168	131	174	76	3	80	CCR5xCD3(VH7/VL2)	HLHL
15	131	168	129	174	80	3	76	CCR5xCD3 (VL2/ VH7)	LHLH
16	129	168	131	174	80	3	76	CCR5xCD3(VL2/ VH7)	HLLH

Table 6B Deimmunized anti-human CD3 constructs comprising single chain anti-CCR5 variable regions: nucleic acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	173	128	201	130	CD3 (VL2/ VH5) xCCR5	LHHL
2	73	202	79	173	128	201	130	CD3 (VH5/VL2) xCCR5	HLHL
3	79	202	73	173	130	201	128	CD3 (VL2/ VH5) xCCR5	LHLH
4	73	202	79	173	130	201	128	CD3 (VH5/VL2) xCCR5	HLLH
5	130	201	128	173	73	202	79	CCR5xCD3 (VH5/VL2)	LHHL
6	128	201	130	173	73	202	79	CCR5xCD3(VH5/VL2)	HLHL
7	130	201	128	173	79	202	73	CCR5xCD3 (VL2/ VH5)	LHLH
8	128	201	130	173	79	202	73	CCR5xCD3(VL2/ VH5)	HLLH
9	79	202	75	173	128	201	130	CD3 (VL2/ VH7) xCCR5	LHHL
10	75	202	79	173	128	201	130	CD3 (VH7/VL2) xCCR5	HLHL
11	79	202	75	173	130	201	128	CD3 (VL2/ VH7) xCCR5	LHLH
12	75	202	79	173	130	201	128	CD3 (VH7/VL2) xCCR5	HLLH
13	130	201	128	173	75	202	79	CCR5xCD3 (VH7/VL2)	LHHL
14	128	201	130	173	75	202	79	CCR5xCD3(VH7/VL2)	HLHL
15	130	201	128	173	79	202	75	CCR5xCD3 (VL2/ VH7)	LHLH
16	128	201	130	173	79	202	75	CCR5xCD3 (VL2/ VH7)	HLLH

Preferably, said constructs comprise an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO 206, 208, 210, 212, 214 or 216;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 205, 207, 209, 211, 213 or 215; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

The CCR5 and CD3 binding constructs 206, 208, 210 represent construct 5 and SEQ ID NO.:212, 214 and 216 represent construct 13 of Table 6 and have the three different VL regions (VL1 (SEQ ID NO.:78), VL2 (SEQ ID NO.:80), or VL3 (SEQ ID NO.:82).

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to CCR5, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NO 205, 207, 209, 211, 213 or 215 under stringent hybridization conditions. The terms "hybridization" and "stringent conditions" have been described herein above. The corresponding definitions and embodiments apply here mutatis mutantis.

The deimmunized CD3 and CCR5 binding constructs provided herein are particularly useful in the medical intervention of viral disease, in particular HIV infections and AIDS, or of autoimmune diseases and/or inflammatory diseases, like rheumatoid arthritis.

In another embodiment, the present invention provides for CD3 specific binding constructs as defined herein above, wherein the Ig-derived second domain of the inventive construct comprises an antigen-interaction site with specificity for CD19.

CD19 has proved to be a very useful medical target. CD19 is expressed in the whole B lineage from the pro B cell to the mature B cell, it is not shed, is uniformly expressed on all lymphoma cells, and is absent from stem cells (Haagen, Clin Exp Immunol 90 (1992), 368-75; Uckun, Proc. Natl. Acad. Sci. USA 85 (1988), 8603-7). Combination therapy employing both an antibody directed against CD19 and an additional immunoregulatory antibody has been disclosed for the treatment of B cell malignancies (WO 02/04021, US2002006404, US2002028178) and autoimmune diseases (WO 02/22212, US2002058029). WO 00/67795 discloses the use i.a. of antibodies directed against CD19 for the treatment of indolent and aggressive forms of B-cell lymphomas, as well as acute and chronic forms of lymphatic leukemias. WO 02/80987 discloses the therapeutic use of immunotoxins based on antibodies against the antigen CD19 for the treatment of such diseases as B cell non-Hodgkin's lymphoma, Hodgkin's lymphoma or B cell leukemias (e.g. B cell acute lymphatic leukemia (B-ALL), (e.g. hairy cell lymphoma) B cell precursor acute lymphatic leukemia (pre-B-ALL), B cell chronic lymphatic leukemia (B-CLL)) .

In a particularly preferred embodiment of the present invention, CD3-specific binding constructs are provided, which comprise an deimmunized domain directed against/binding to/interacting with human CD3 and a second Ig-derived domain which specifically binds to/interacts with CD19. Such constructs are shown in Table 7A and 7B. The modules A-G in Tables 7A and 7B can be defined as mentioned above for Tables 1-5. Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 78, 80 or 82. The VH protein domain of human CD19 antibody is as set out in SEQ ID NO: 114. The VL protein domain of human CCR5 antibody is as set out in SEQ ID NO: 116. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out

in SEQ ID NO: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the CD19 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 168. The respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 174. However, as mentioned above an additional serine may be introduced for cloning purposes (linker as depicted in SEQ ID NO.:176) between the VL and subsequente V domain.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 77, 79 or 81. The nucleic acid molecule encoding the VH protein domain of the human CD19 antibody is as set out in SEQ ID NO: 113. The nucleic acid molecule encoding the VL protein domain of the human CCR5 antibody is as set out in SEQ ID NO: 115. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 202. When either the module pair A/C or E/G denotes a nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the CD19 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO: 201. The groups of nucleic acid modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 173. An alternative linker SEQ ID NO.:175 may also be used to conjugate VL domain with a subsequent V domain (including an additional codon encoding a serine residue for cloning purposes).

Table 7A Deimmunized anti-human CD3 constructs comprising single chain anti-CD19 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	174	114	168	116	CD3 (VL2/ VH5) xCD19	LHHL
2	74	3	80	174	114	168	116	CD3 (VH5/VL2) xCD19	HLHL
3	80	3	74	174	116	168	114	CD3 (VL2/ VH5) xCD19	LHLH
4	74	3	80	174	116	168	114	CD3 (VH5/VL2) xCD19	HLLH
5	116	168	114	174	74	3	80	CD19xCD3 (VH5/VL2)	LHHL
6	114	168	116	174	74	3	80	CD19xCD3(VH5/VL2)	HLHL
7	116	168	114	174	80	3	74	CD19xCD3 (VL2/ VH5)	LHLH
8	114	168	116	174	80	3	74	CD19xCD3(VL2/ VH5)	HLLH
9	80	3	76	174	114	168	116	CD3 (VL2/ VH7) xCD19	LHHL
10	76	3	80	174	114	168	116	CD3 (VH7/VL2) xCD19	HLHL
11	80	3	76	174	116	168	114	CD3 (VL2/ VH7) xCD19	LHLH
12	76	3	80	174	116	168	114	CD3 (VH7/VL2) xCD19	HLLH
13	116	168	114	174	76	3	80	CD19xCD3 (VH7/VL2)	LHHL
14	114	168	116	174	76	3	80	CD19xCD3(VH7/VL2)	HLHL
15	116	168	114	174	80	3	76	CD19xCD3 (VL2/ VH7)	LHLH
16	114	168	116	174	80	3	76	CD19xCD3(VL2/ VH7)	HLLH

Table 7B Deimmunized anti-human CD3 constructs comprising single chain anti-CD19 variable regions: Nucleic acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	173	113	201	115	CD3 (VL2/ VH5) xCD19	LHHL
2	73	202	79	173	113	201	115	CD3 (VH5/VL2) xCD19	HLHL
3	79	202	73	173	115	201	113	CD3 (VL2/ VH5) xCD19	LHLH
4	73	202	79	173	115	201	113	CD3 (VH5/VL2) xCD19	HLLH
5	115	201	113	173	73	202	79	CD19xCD3 (VH5/VL2)	LHHL
6	113	201	115	173	73	202	79	CD19xCD3(VH5/VL2)	HLHL
7	115	201	113	173	79	202	73	CD19xCD3 (VL2/ VH5)	LHLH
8	113	201	115	173	79	202	73	CD19xCD3(VL2/ VH5)	HLLH
9	79	202	75	173	113	201	115	CD3 (VL2/ VH7) xCD19	LHHL
10	75	202	79	173	113	201	115	CD3 (VH7/VL2) xCD19	HLHL
11	79	202	75	173	115	201	113	CD3 (VL2/ VH7) xCD19	LHLH
12	75	202	79	173	115	201	113	CD3 (VH7/VL2) xCD19	HLLH
13	115	201	113	173	75	202	79	CD19xCD3 (VH7/VL2)	LHHL
14	113	201	115	173	75	202	79	CD19xCD3(VH7/VL2)	HLHL
15	115	201	113	173	79	202	75	CD19xCD3 (VL2/ VH7)	LHLH
16	113	201	115	173	79	202	75	CD19xCD3(VL2/ VH7)	HLLH

In a more preferred embodiment, the present invention provides for a deimmunized CD3-specific binding construct which comprises a CD3-binding domain as defined above and a second, Ig-derived domain which specifically binds to /interacts with CD19, preferably human CD19, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO 190, 192, 194, 196, 198, 200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 189, 191, 193, 195, 197,199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406 or 408; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

Preferred CD19 and CD3 binding constructs according to the invention are SEQ ID NO.:190, 192, 194 representing construct 5 and SEQ ID NO.:196, 198 and 200 representing construct 13 of Table 7 and having the three different VL regions (VL1 (SEQ ID NO.:78), VL2 (SEQ ID NO.:80), or VL3 (SEQ ID NO.:82)).

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to CD19, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NOs: 189, 191, 193, 195, 197,199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398,

400, 402, 404, 406 or 408, under stringent hybridization conditions. The terms "hybridization" and "stringent conditions" have been described herein above. The corresponding definitions and embodiments apply here mutatis mutantis.

The herein disclosed deimmunized CD3 and CD19 binding constructs are particularly useful in the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, a viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases, host-versus-graft diseases or B-cell malignancies, in particular B cell non-Hodgkin's lymphoma, Hodgkin's lymphoma or B cell leukemias (e.g. B cell acute lymphoatic leukemia (B-ALL), (e.g. hairy cell lymphoma) B cell precursor acute lymphatic leukemia (pre-B-ALL), B cell chronic lymphatic leukemia (B-CLL)) leukemia.

In a further embodiment, the present invention relates to a CD3 specific binding construct as defined above comprising a first domain specifically binding to human CD3 and having reduced propensity to generate T cell epitopes and a second domain, wherein said second domain is Ig-derived and comprises an antigen-interaction site with a specificity for CD20.

CD20 is one of the cell surface proteins present on B-lymphocytes. CD20 antigen is found in normal and malignant pre-B and mature B lymphocytes, including those in over 90% of B-cell non-Hodgkin's lymphomas (NHL). The antigen is absent in hematopoetic stem cells, activated B lymphocytes (plasma cells) and normal tissue. Several antibodies mostly of murine origin have been described: 1F5 (Press et al., 1987, Blood 69/2, 584-591), 2B8 / C2B8, 2H7, 1H4 (Liu et al., 1987, J Immunol 139, 3521-3526; Anderson et al., 1998, US patent No. 5,736,137; Haisma et al., 1998, Blood 92, 184-190; Shan et al., 1999, J. Immunol 162, 6589-6595).

CD20 has been described in immunotherapeutic strategies for the treatment of plasma cell malignancies using vaccination with DNA encoding scFv linked to carrier protein (Treon et al., 2000, Semin Oncol 27(5), 598) and in immunotherapeutic treatment using CD20 antibodies (IDEC-C2B8) have been shown to be effective in the treatment of non-Hodgkin's B-cell lymphoma. CD20 antibodies have proven

efficacy and tolerability in non-Hodgkin's lymphoma, achieving response rates of 73% and 48% in previously untreated or relapsed/refractory indolent non-Hodgkin's lymphoma, respectively (Montserrat, 2003, Semin Oncol 30(1suppl2), 34-39). Furthermore, CD20 antibodies have been widely used to treat relapsing or advanced stage B-cell neoplasms with an efficacy of about 50%.

In a particularly preferred embodiment of the present invention, CD3-specific binding constructs are provided, which comprise a deimmunized domain directed against/binding to/interacting with human CD3 and a second Ig-derived domain which specifically binds to/interacts with CD20. Such constructs are shown in Table 8A and 8B. The modules A-G in Tables 8A and 8B can be defined as mentioned above for Tables 1-5. Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 78, 80 or 82. The VH protein domain of human CD20 antibody is as set out in SEQ ID NO: 170. The VL protein domain of human CD20 antibody is as set out in SEQ ID NO: 172. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the CD20 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 168. The respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 174. However, as mentioned above an additional serine may be introduced for cloning purposes (linker as depicted in SEQ ID NO.:176) between the VL and subsequent V domain.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 77, 79 or 81. The nucleic acid

molecule encoding the VH protein domain of the human CD20 antibody is as set out in SEQ ID NO: 169. The nucleic acid molecule encoding the VL protein domain of the human CD20 antibody is as set out in SEQ ID NO: 171. When either the module pair A/C or E/G denotes a nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 202. When either the module pair A/C or E/G denotes a nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the CD20 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO: 201. The groups of nucleic acid modules A-B-C and E-F-G are connected to each other through nucleic acid module D, having the sequence as set out in SEQ ID NO: 173. An alternative linker SEQ ID NO.:175 may also be used to conjugate VL domain with a subsequent V domain (including an additional codon encoding a serine residue for cloning purposes).

Table 8A Deimmunized anti-human CD3 constructs comprising single chain anti-CD20 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	174	170	168	172	CD3 (VL2/ VH5) xCD20	LHHL
2	74	3	80	174	170	168	172	CD3 (VH5/VL2) xCD20	HLHL
3	80	3	74	174	172	168	170	CD3 (VL2/ VH5) xCD20	LHLH
4	74	3	80	174	172	168	170	CD3 (VH5/VL2) xCD20	HLLH
5	172	168	170	174	74	3	80	CD20xCD3 (VH5/VL2)	LHHL
6	170	168	172	174	74	3	80	CD20xCD3(VH5/VL2)	HLHL
7	172	168	170	174	80	3	74	CD20xCD3 (VL2/ VH5)	LHLH
8	170	168	172	174	80	3	74	CD20xCD3(VL2/ VH5)	HLLH
9	80	3	76	174	170	168	172	CD3 (VL2/ VH7) xCD20	LHHL
10	76	3	80	174	170	168	172	CD3 (VH7/VL2) xCD20	HLHL
11	80	3	76	174	172	168	170	CD3 (VL2/ VH7) xCD20	LHLH
12	76	3	80	174	172	168	170	CD3 (VH7/VL2) xCD20	HLLH
13	172	168	170	174	76	3	80	CD20xCD3 (VH7/VL2)	LHHL
14	170	168	172	174	76	3	80	CD20xCD3(VH7/VL2)	HLHL
15	172	168	170	174	80	3	76	CD20xCD3 (VL2/ VH7)	LHLH
16	170	168	172	174	80	3	76	CD20xCD3(VL2/ VH7)	HLLH

Table 8B Deimmunized anti-human CD3 constructs comprising single chain anti-CD20 variable regions: Nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	173	169	201	171	CD3 (VL2/ VH5) xCD20	LHHL
2	73	202	79	173	169	201	171	CD3 (VH5/VL2) xCD20	HLHL
3	79	202	73	173	171	201	169	CD3 (VL2/ VH5) xCD20	LHLH
4	73	202	79	173	171	201	169	CD3 (VH5/VL2) xCD20	HLLH
5	171	201	169	173	73	202	79	CD20xCD3 (VH5/VL2)	LHHL
6	169	201	171	173	73	202	79	CD20xCD3(VH5/VL2)	HLHL
7	171	201	169	173	79	202	73	CD20xCD3 (VL2/ VH5)	LHLH
8	169	201	171	173	79	202	73	CD20xCD3(VL2/ VH5)	HLLH
9	79	202	75	173	169	201	171	CD3 (VL2/ VH7) xCD20	LHHL
10	75	202	79	173	169	201	171	CD3 (VH7/VL2) xCD20	HLHL
11	79	202	75	173	171	201	169	CD3 (VL2/ VH7) xCD20	LHLH
12	75	202	79	173	171	201	169	CD3 (VH7/VL2) xCD20	HLLH
13	171	201	169	173	75	202	79	CD20xCD3 (VH7/VL2)	LHHL
14	169	201	171	173	75	202	79	CD20xCD3(VH7/VL2)	HLHL
15	171	201	169	173	79	202	75	CD20xCD3 (VL2/ VH7)	LHLH
16	169	201	171	173	79	202	75	CD20xCD3(VL2/ VH7)	HLLH

More preferably, the deimmunized CD3 and CD20 binding constructs of the present invention comprises an amino acid sequence which is selected from the group consisting of

(a) an amino acid sequence as shown in any one of SEQ ID NO 218, 220, 222, 224, 226, or 228 ;
(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 217, 219, 221, 223, 225 or 227; and
(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b) ;
(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to CD20, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NO 217, 219, 221, 223, 225 or 227, under stringent hybridization conditions. The terms "hybridization" and "stringent conditions" have been described herein above. The corresponding definitions and embodiments apply here mutatis mutantis.

The herein described deimmunized CD3 and CD20 binding constructs are envisaged for use in the treatment, prevention and/or amelioration of B-cell related disorders, preferably in the medical intervention of lymphoma, more preferably in the treatment of non-Hodgkin lymphoma.

The invention also provides for nucleic acid sequence encoding a CD3 specific binding molecule of the invention.

It is evident to the person skilled in the art that regulatory sequences may be added to the nucleic acid molecule of the invention. For example, promoters, transcriptional

enhancers and/or sequences which allow for induced expression of the polynucleotide of the invention may be employed. A suitable inducible system is for example tetracycline-regulated gene expression as described, e.g., by Gossen and Bujard (Proc. Natl. Acad. Sci. USA 89 (1992), 5547-5551) and Gossen et al. (Trends Biotech. 12 (1994), 58-62), or a dexamethasone-inducible gene expression system as described, e.g. by Crook (1989) EMBO J. 8, 513-519 .

Furthermore, it is envisaged for further purposes that nucleic acid molecules may contain, for example, thioester bonds and/or nucleotide analogues. Said modifications may be useful for the stabilization of the nucleic acid molecule against endo- and/or exonucleases in the cell. Said nucleic acid molecules may be transcribed by an appropriate vector containing a chimeric gene which allows for the transcription of said nucleic acid molecule in the cell. In this respect, it is also to be understood that such polynucleotide can be used for "gene targeting" or "gene therapeutic" approaches. In another embodiment said nucleic acid molecules are labeled. Methods for the detection of nucleic acids are well known in the art, e.g., Southern and Northern blotting, PCR or primer extension. This embodiment may be useful for screening methods for verifying successful introduction of the nucleic acid molecules described above during gene therapy approaches.

Said nucleic acid molecule(s) may be a recombinantly produced chimeric nucleic acid molecule comprising any of the aforementioned nucleic acid molecules either alone or in combination. Preferably, the nucleic acid molecule is part of a vector.

The present invention therefore also relates to a vector comprising the nucleic acid molecule described in the present invention.
Many suitable vectors are known to those skilled in molecular biology, the choice of which would depend on the function desired and include plasmids, cosmids, viruses, bacteriophages and other vectors used conventionally in genetic engineering. Methods which are well known to those skilled in the art can be used to construct various plasmids and vectors; see, for example, the techniques described in Sambrook et al. (loc cit.) and Ausubel, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. (1989), (1994). Alternatively, the polynucleotides and vectors of the invention can be reconstituted into liposomes for

delivery to target cells. As discussed in further details below, a cloning vector was used to isolate individual sequences of DNA. Relevant sequences can be transferred into expression vectors where expression of a particular polypeptide is required. Typical cloning vectors include pBluescript SK, pGEM, pUC9, pBR322 and pGBT9. Typical expression vectors include pTRE, pCAL-n-EK, pESP-1, pOP13CAT.

Preferably said vector comprises a nucleic acid sequence which is a regulatory sequence operably linked to said nucleic acid sequence encoding a bispecific single chain antibody constructs defined herein.

Such regulatory sequences (control elements) are known to the artisan and may include a promoter, a splice cassette, translation initiation codon, translation and insertion site for introducing an insert into the vector. Preferably, said nucleic acid molecule is operatively linked to said expression control sequences allowing expression in eukaryotic or prokaryotic cells.

It is envisaged that said vector is an expression vector comprising the nucleic acid molecule encoding a bispecific single chain antibody constructs defined herein.

The term "regulatory sequence" refers to DNA sequences, which are necessary to effect the expression of coding sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism. In prokaryotes, control sequences generally include promoter, ribosomal binding site, and terminators. In eukaryotes generally control sequences include promoters, terminators and, in some instances, enhancers, transactivators or transcription factors. The term "control sequence" is intended to include, at a minimum, all components the presence of which are necessary for expression, and may also include additional advantageous components.

The term "operably linked" refers to a juxtaposition wherein the components so described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences. In case the control sequence is a promoter, it is obvious for a skilled person that double-stranded nucleic acid is preferably used.

Thus, the recited vector is preferably an expression vector. An "expression vector" is a construct that can be used to transform a selected host and provides for expression of a coding sequence in the selected host. Expression vectors can for instance be cloning vectors, binary vectors or integrating vectors. Expression comprises

transcription of the nucleic acid molecule preferably into a translatable mRNA. Regulatory elements ensuring expression in prokaryotes and/or eukaryotic cells are well known to those skilled in the art. In the case of eukaryotic cells they comprise normally promoters ensuring initiation of transcription and optionally poly-A signals ensuring termination of transcription and stabilization of the transcript. Possible regulatory elements permitting expression in prokaryotic host cells comprise, e.g., the P_L, *lac*, *trp* or *tac* promoter in *E. coli*, and examples of regulatory elements permitting expression in eukaryotic host cells are the *AOX1* or *GAL1* promoter in yeast or the CMV-, SV40-, RSV-promoter (Rous sarcoma virus), CMV-enhancer, SV40-enhancer or a globin intron in mammalian and other animal cells.
Beside elements which are responsible for the initiation of transcription such regulatory elements may also comprise transcription termination signals, such as the SV40-poly-A site or the tk-poly-A site, downstream of the polynucleotide. Furthermore, depending on the expression system used leader sequences capable of directing the polypeptide to a cellular compartment or secreting it into the medium may be added to the coding sequence of the recited nucleic acid sequence and are well known in the art; see also, e.g., appended example 1. The leader sequence(s) is (are) assembled in appropriate phase with translation, initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein, or a portion thereof, into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an N-terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product; see supra. In this context, suitable expression vectors are known in the art such as Okayama-Berg cDNA expression vector pcDV1 (Pharmacia), pCDM8, pRc/CMV, pcDNA1, pcDNA3 (In-vitrogene), pEF-DHFR, pEF-ADA or pEF-neo (Raum et al. Cancer Immunol Immunother (2001) 50(3), 141-150) or pSPORT1 (GIBCO BRL).

Preferably, the expression control sequences will be eukaryotic promoter systems in vectors capable of transforming of transfecting eukaryotic host cells, but control sequences for prokaryotic hosts may also be used. Once the vector has been incorporated into the appropriate host, the host is maintained under conditions suitable for high level expression of the nucleotide sequences, and as desired, the collection and purification of the polypeptide of the invention may follow; see, e.g.,

the appended examples.

An alternative expression system which could be used to express a cell cycle interacting protein is an insect system. In one such system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The coding sequence of a recited nucleic acid molecule may be cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of said coding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein coat. The recombinant viruses are then used to infect *S. frugiperda* cells or *Trichoplusia* larvae in which the protein of the invention is expressed (Smith, J. Virol. 46 (1983), 584; Engelhard, Proc. Nat. Acad. Sci. USA 91 (1994), 3224-3227).

Additional regulatory elements may include transcriptional as well as translational enhancers. Advantageously, the above-described vectors of the invention comprises a selectable and/or scorable marker.

Selectable marker genes useful for the selection of transformed cells and, e.g., plant tissue and plants are well known to those skilled in the art and comprise, for example, antimetabolite resistance as the basis of selection for dhfr, which confers resistance to methotrexate (Reiss, Plant Physiol. (Life Sci. Adv.) 13 (1994), 143-149); npt, which confers resistance to the aminoglycosides neomycin, kanamycin and paromycin (Herrera-Estrella, EMBO J. 2 (1983), 987-995) and hygro, which confers resistance to hygromycin (Marsh, Gene 32 (1984), 481-485). Additional selectable genes have been described, namely trpB, which allows cells to utilize indole in place of tryptophan; hisD, which allows cells to utilize histinol in place of histidine (Hartman, Proc. Natl. Acad. Sci. USA 85 (1988), 8047); mannose-6-phosphate isomerase which allows cells to utilize mannose (WO 94/20627) and ODC (ornithine decarboxylase) which confers resistance to the ornithine decarboxylase inhibitor, 2-(difluoromethyl)-DL-ornithine, DFMO (McConlogue, 1987, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory ed.) or deaminase from Aspergillus terreus which confers resistance to Blasticidin S (Tamura, Biosci. Biotechnol. Biochem. 59 (1995), 2336-2338).

Useful scorable markers are also known to those skilled in the art and are commercially available. Advantageously, said marker is a gene encoding luciferase (Giacomin, Pl. Sci. 116 (1996), 59-72; Scikantha, J. Bact. 178 (1996), 121), green

fluorescent protein (Gerdes, FEBS Lett. 389 (1996), 44-47) or ß-glucuronidase (Jefferson, EMBO J. 6 (1987), 3901-3907). This embodiment is particularly useful for simple and rapid screening of cells, tissues and organisms containing a recited vector.

As described above, the recited nucleic acid molecule can be used alone or as part of a vector to express the encoded CD3 specific construct in cells, for, e.g., purification but also for gene therapy purposes. The nucleic acid molecules or vectors containing the DNA sequence(s) encoding any one of the above described (bispecific) CD3 constructs is introduced into the cells which in turn produce the polypeptide of interest. Gene therapy, which is based on introducing therapeutic genes into cells by ex-vivo or in-vivo techniques is one of the most important applications of gene transfer. Suitable vectors, methods or gene-delivery systems for in-vitro or in-vivo gene therapy are described in the literature and are known to the person skilled in the art; see, e.g., Giordano, Nature Medicine 2 (1996), 534-539; Schaper, Circ. Res. 79 (1996), 911-919; Anderson, Science 256 (1992), 808-813; Verma, Nature 389 (1994), 239; Isner, Lancet 348 (1996), 370-374; Muhlhauser, Circ. Res. 77 (1995), 1077-1086; Onodera, Blood 91 (1998), 30-36; Verma, Gene Ther. 5 (1998), 692-699; Nabel, Ann. N.Y. Acad. Sci. 811 (1997), 289-292; Verzeletti, Hum. Gene Ther. 9 (1998), 2243-51; Wang, Nature Medicine 2 (1996), 714-716; WO 94/29469; WO 97/00957, US 5,580,859; US 5,589,466; or Schaper, Current Opinion in Biotechnology 7 (1996), 635-640. The recited nucleic acid molecules and vectors may be designed for direct introduction or for introduction via liposomes, or viral vectors (e.g., adenoviral, retroviral) into the cell. Preferably, said cell is a germ line cell, embryonic cell, or egg cell or derived therefrom, most preferably said cell is a stem cell. An example for an embryonic stem cell can be, inter alia, a stem cell as described in, Nagy, Proc. Natl. Acad. Sci. USA 90 (1993), 8424-8428.

In accordance with the above, the present invention relates to methods to derive vectors, particularly plasmids, cosmids, viruses and bacteriophages used conventionally in genetic engineering that comprise a nucleic acid molecule encoding the polypeptide sequence of a bispecific single chain antibody constructs defined herein. Preferably, said vector is an expression vector and/or a gene transfer or targeting vector. Expression vectors derived from viruses such as retroviruses, vaccinia virus, adeno-associated virus, herpes viruses, or bovine papilloma virus,

may be used for delivery of the recited polynucleotides or vector into targeted cell populations. Methods which are well known to those skilled in the art can be used to construct recombinant vectors; see, for example, the techniques described in Sambrook et al. (loc cit.), Ausubel (1989, loc cit.) or other standard text books. Alternatively, the recited nucleic acid molecules and vectors can be reconstituted into liposomes for delivery to target cells. The vectors containing the nucleic acid molecules of the invention can be transferred into the host cell by well-known methods, which vary depending on the type of cellular host. For example, calcium chloride transfection is commonly utilized for prokaryotic cells, whereas calcium phosphate treatment or electroporation may be used for other cellular hosts; see Sambrook, supra.

The recited vector may, inter alia, be the pEF-DHFR, pEF-ADA or pEF-neo. The vectors pEF-DHFR, pEF-ADA and pEF-neo have been described in the art, e.g. in Mack et al. (PNAS (1995) 92, 7021-7025) and Raum et al. (Cancer Immunol Immunother (2001) 50(3), 141-150).

The invention also provides for a host transformed or transfected with a vector as described herein. Said host may be produced by introducing said at least one of the above described vector or at least one of the above described nucleic acid molecules into the host. The presence of said at least one vector or at least one nucleic acid molecule in the host may mediate the expression of a gene encoding the above described bispecific single chain antibody constructs.

The described nucleic acid molecule or vector which is introduced in the host may either integrate into the genome of the host or it may be maintained extrachromosomally.

The host can be any prokaryote or eukaryotic cell.

The term "prokaryote" is meant to include all bacteria which can be transformed or transfected with DNA or RNA molecules for the expression of a protein of the invention. Prokaryotic hosts may include gram negative as well as gram positive bacteria such as, for example, E. coli, S. typhimurium, Serratia marcescens and Bacillus subtilis. The term "eukaryotic" is meant to include yeast, higher plant, insect and preferably mammalian cells. Depending upon the host employed in a recombinant production procedure, the protein encoded by the polynucleotide of the present invention may be glycosylated or may be non-glycosylated. Especially

preferred is the use of a plasmid or a virus containing the coding sequence of the polypeptide of the invention and genetically fused thereto an N-terminal FLAG-tag and/or C-terminal His-tag. Preferably, the length of said FLAG-tag is about 4 to 8 amino acids, most preferably 8 amino acids. An above described polynucleotide can be used to transform or transfect the host using any of the techniques commonly known to those of ordinary skill in the art. Furthermore, methods for preparing fused, operably linked genes and expressing them in, e.g., mammalian cells and bacteria are well-known in the art (Sambrook, loc cit.).

Preferably, said the host is a bacteria, an insect, fungal, plant or animal cell.

It is particularly envisaged that the recited host may be a mammalian cell, more preferably a human cell or human cell line.

Particularly preferred host cells comprise CHO cells, COS cells, myeloma cell lines like SP2/0 or NS/0. As illustrated in the appended examples, particularly preferred are CHO-cells as hosts.

In a further embodiment, the present invention thus relates to a process for the preparation of a CD3 specific construct described above comprising cultivating a cell and/or the host of the invention under conditions suitable for the expression of said construct and isolating the construct from the cell or the culture medium.

The transformed hosts can be grown in fermentors and cultured according to techniques known in the art to achieve optimal cell growth. The polypeptide of the invention can then be isolated from the growth medium, cellular lysates, or cellular membrane fractions. The isolation and purification of the, e.g., microbially expressed polypeptides of the invention may be by any conventional means such as, for example, preparative chromatographic separations and immunological separations such as those involving the use of monoclonal or polyclonal antibodies directed, e.g., against a tag of the polypeptide of the invention or as described in the appended examples.

Furthermore, the invention provides for a composition comprising a (human) CD3-specific binding construct as defined herein or a (human) CD3-specific binding construct as produced by the process disclosed above, a nucleic acid molecule of the invention, a vector or a host of the invention. Said composition may, optionally, also comprise a proteinaceous compound capable of providing an activation signal for

immune effector cells. Most preferably, said composition is a pharmaceutical composition further comprising, optionally, suitable formulations of carrier, stabilizers and/or excipients.

In accordance with this invention, the term "pharmaceutical composition" relates to a composition for administration to a patient, preferably a human patient. In a preferred embodiment, the pharmaceutical composition comprises a composition for parenteral, transdermal, intraluminal, intra arterial, intrathecal administration or by direct injection into the tissue or tumour. It is in particular envisaged that said pharmaceutical composition is administered to a patient via infusion or injection. Administration of the suitable compositions may be effected by different ways, e.g., by intravenous, intraperitoneal, subcutaneous, intramuscular, topical or intradermal administration. The pharmaceutical composition of the present invention may further comprise a pharmaceutically acceptable carrier. Examples of suitable pharmaceutical carriers are well known in the art and include phosphate buffered saline solutions, water, emulsions, such as oil/water emulsions, various types of wetting agents, sterile solutions, etc. Compositions comprising such carriers can be formulated by well known conventional methods. These pharmaceutical compositions can be administered to the subject at a suitable dose. The dosage regimen will be determined by the attending physician and clinical factors. As is well known in the medical arts, dosages for any one patient depends upon many factors, including the patient's size, body surface area, age, the particular compound to be administered, sex, time and route of administration, general health, and other drugs being administered concurrently. Generally, the regimen as a regular administration of the pharmaceutical composition should be in the range of 1 µg to 5 g units per day. However, a more preferred dosage for continuous infusion might be in the range of 0.01 µg to 2 mg, preferably 0.01 µg to 1 mg, more preferably 0.01 µg to 100 µg, even more preferably 0.01 µg to 50 µg and most preferably 0.01 µg to 10 µg units per kilogram of body weight per hour. Particularly preferred dosages are recited herein below. Progress can be monitored by periodic assessment. Dosages will vary but a preferred dosage for intravenous administration of DNA is from approximately 10^6 to 10^{12} copies of the DNA molecule. The compositions of the invention may be administered locally or systematically. Administration will generally be parenterally, e.g., intravenously; DNA may also be administered directed to the target site, e.g., by

biolistic delivery to an internal or external target site or by catheter to a site in an artery. Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's, or fixed oils. Intravenous vehicles include fluid and nutrient replenishes, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, and inert gases and the like. In addition, the pharmaceutical composition of the present invention might comprise proteinaceous carriers, like, e.g., serum albumine or immunoglobuline, preferably of human origin. It is envisaged that the pharmaceutical composition of the invention might comprise, in addition to the proteinaceous bispecific single chain antibody constructs or nucleic acid molecules or vectors encoding the same (as described in this invention), further biologically active agents, depending on the intended use of the pharmaceutical composition. Such agents might be drugs acting on the gastro-intestinal system, drugs acting as cytostatica, drugs preventing hyperurikemia, drugs inhibiting immunereactions (e.g. corticosteroids), drugs acting on the circulatory system and/or agents such as T-cell co-stimulatory molecules or cytokines known in the art.

Possible indications for administration of the composition(s) of the invention are tumorous diseases especially epithelial cancers/carcinomas such as breast cancer, colon cancer, prostate cancer, head and neck cancer, skin cancer (melanoma), cancers of the genito-urinary tract, e.g. ovarial cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer, cancers of the bile duct, esophagus cancer, cancer of the salivatory glands and cancer of the thyroid gland or other tumorous diseases like haematological tumors, gliomas, sarcomas or osteosarcomas. The administration of the composition(s) of the invention is especially indicated for minimal residual disease, preferably early solid tumors, advanced solid tumors or metatatic solid tumors, which is characterized by the local and non-local reoccurrance of the tumor caused by the survival of single cells.

The invention further envisages the co-administration protocols with other compounds, e.g. molecules capable of providing an activation signal for immune effector cells, for cell proliferation or for cell stimulation. Said molecule may be, e.g. a further primary activation signal for T cells (e.g. a further costimulatory molecule: molecules of B7 family, Ox40L, 4.1 BBL), or a further cytokine: interleukin (e.g. IL-2) or NKG-2D engaging compound.

The composition of the invention as described above may also be a diagnostic composition further comprising, optionally, means and methods for detection.

The CD3-specific constructs provided herein are also suited for use in immunoassays in which they can be utilized in liquid phase or bound to a solid phase carrier. Examples of immunoassays which can utilize the polypeptide of the invention are competitive and non-competitive immunoassays in either a direct or indirect format. Examples of such immunoassays are the enzyme linked immunosorbent assa (ELISA), enzyme immunoassay (EIA) , radioimmunoassay (RIA), the sandwich (immunometric assay) and the Western blot assay.
The CD3 specific binding constructs of the invention can be bound to many different carriers and used to isolate cells specifically bound to said polypeptides. Examples of well-known carriers include glass, polystyrene, polyvinyl chloride, polypropylene, polyethylene, polycarbonate, dextran, nylon, amyloses, natural and modified celluloses, polyacrylamides, agaroses, and magnetite. The nature of the carrier can be either soluble or insoluble, e.g. as beads, for the purposes of the invention.

There are many different labels and methods of labeling known to those of ordinary skill in the art. Examples of the types of labels which can be used in the present invention include enzymes, radioisotopes, colloidal metals, fluorescent compounds, chemiluminescent compounds, and bioluminescent compounds; see also the embodiments discussed hereinabove.

In a most preferred embodiment of the present invention, the use of a CD3 specific binding molecule of the invention, of a vector or of a host of the invention for the preparation of a pharmaceutical composition is envisaged. Said pharmaceutical composition may be employed in the prevention, treatment or amelioration of a

proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases.

Furthermore, in accordance to the invention, the deimmunized constructs comprising CD19 and CD3 binding domains, preferably SEQ ID NO.190, 192, 194, 196, 198, 200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409, can be used for the treatment of immunological disorders (various B cell malignancies) or autoimmune diseases, the deimmunized constructs comprising CCR5 and CD3 binding domains, preferably SEQ ID NO.206, 208, 210, 212, 214 or 216, can be used for the treatment of viral diseases (HIV), autoimmune diseases and/or of inflammatory diseases (like rheumatoid arthritis), the deimmunized constructs comprising CD20 and CD3 binding domains, preferably SEQ ID NO.218, 220, 222, 224, 226, 228, can be used for the treatment of tumorous diseases, preferably lymphoma, more preferably non-Hodgkin's B-cell lymphoma and the deimmunized constructs comprising EpCAM and CD3 binding domains, preferably SEQ ID NO.31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 or 325 can be used for the treatment of tumorous diseases, preferably epithelial cancers.

The invention also relates to a method for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases comprising the administration of a (bispecific) CD3 specific binding molecule of the invention or a (bispecific) CD3 specific binding molecule as produced by the process described herein, of a nucleic acid molecule, a vector or a host of the invention to a subject in need of such a prevention, treatment or amelioration . Preferably, said subject is a human.

The method for the prevention, treatment or amelioration may also, in addition, comprise the administration of a proteinaceous compound capable of providing an activation signal for immune effector cells. Said proteinaceous compound may be administered simultaneously or non-simultaneously with the CD3 binding molecule, a nucleic acid molecule, a vector or a host of the invention. The proteinaceous compound may, inter alia, selected from the group consisting of a further costimulatory molecule:molecules of B7 family, Ox40L, 4.1 BBL), or a further cytokine: interleukin (e.g. IL-2) or NKG-2D engaging compounds.

Finally, the invention provides for a kit comprising the CD3 specific binding molecule, a nucleic acid molecule, a vector or a host of the invention.

Said kit is particularly useful in the preparation of the pharmaceutical composition of the present invention and may, inter alia, consist of a container useful for injections or infusions. Advantageously, the kit of the present invention further comprises, optionally (a) buffer(s), storage solutions and/or remaining reagents or materials required for the conduct of medical or scientific purposes. Furthermore, parts of the kit of the invention can be packaged individually in vials or bottles or in combination in containers or multicontainer units. The kit of the present invention may be advantageously used, inter alia, for carrying out the method of the invention and could be employed in a variety of applications referred herein, e.g., as as research tools or medical tools. The manufacture of the kits preferably follows standard procedures which are known to the person skilled in the art.

These and other embodiments are disclosed and encompassed by the description and Examples of the present invention. Further literature concerning any one of the antibodies, methods, uses and compounds to be employed in accordance with the present invention may be retrieved from public libraries and databases, using for example electronic devices. For example, the public database "Medline", available on the Internet, may be utilized, for example under http://www.ncbi.nlm.nih.gov/PubMed/medline.html. Further databases and addresses, such as http://www.ncbi.nlm.nih.gov/, http://www.infobiogen.fr/, http://www.fmi.ch/biology/research_tools.html, http://www.tigr.org/, are known to the person skilled in the art and can also be obtained using, e.g., http://www.lycos.com.

The figures show:

Figure 1. DNA and amino acid sequences of non-deimmunized anti-CD3 cassette (SEQ ID Nos 1 and 2).

Figure 2. A) Amino acid sequences of the heavy chains VH2 (SEQ ID NO.:70), VH3 (SEQ ID NO.:72), VH5 (SEQ ID NO.:74) and VH7 (SEQ ID NO.:76) and light chains VL1 (SEQ ID NO.:78), VL2 (SEQ ID NO.:80) and VL3 (SEQ ID NO.:82), respectively, B) Nucleotide sequences of the heavy chains VH2 (SEQ ID NO.:69), VH3 (SEQ ID NO.:71), VH5 (SEQ ID NO.:73) and VH7 (SEQ ID NO.:75) and light chains VL1 (SEQ ID NO.:77), VL2 (SEQ ID NO.:79) and VL3 (SEQ ID NO.:81), respectively, C) Amino acid sequences of the CDRs 1, 2 and 3 of the heavy chains of the non-deimmunized anti-CD3 (SEQ ID NO.:84, 90, 96, respectively), VH2 (SEQ ID NO.:86, 94, 96, respectively), VH3 (SEQ ID NO.:86, 94, 96, respectively), VH5 (SEQ ID NO.:88, 92, 96, respectively) and VH7 (SEQ ID NO.:88, 90, 96, respectively) and of the light chains of the non-deimmunized anti-CD3 (SEQ ID NO.:98, 102, 104, respectively), chains VL1 (SEQ ID NO.:100, 102, 104, respectively), VL2 (SEQ ID NO.:100, 102, 104, respectively) and VL3 (SEQ ID NO.:98, 102, 104, respectively) and D) Nucleotide sequences of the CDRs 1, 2 and 3 of the heavy chains of the non-deimmunized anti-CD3 (SEQ ID NO.:83, 89, 95, respectively), VH2 (SEQ ID NO.:85, 93, 95, respectively), VH3 (SEQ ID NO.:85, 93, 95, respectively), VH5 (SEQ ID NO.:87, 91, 95, respectively) and VH7 (SEQ ID NO.:87, 89, 95, respectively) and of the light chains of the non-deimmunized anti-CD3 (SEQ ID NO.:97, 101, 103, respectively), chains VL1 (SEQ ID NO.:99, 101, 103, respectively), VL2 (SEQ ID NO.:99, 101, 103, respectively) and VL3 (SEQ ID NO.:97, 101, 103, respectively).

Figure 3. A) Nucleotide sequence of anti-CD3 (VH2/VL1) (SEQ ID NO.:4) B) Amino acid sequence of anti-CD3 (VH2/VL1) (SEQ ID NO.:5) C) Nucleotide sequence of anti-CD3 (VH2/VL2) (SEQ ID NO.:6) D) Amino acid sequence of anti-CD3 (VH2/VL2) (SEQ ID NO.:7) E) Nucleotide sequence of anti-CD3 (VH2/VL3) (SEQ ID NO.:8) F) Amino acid sequence of anti-CD3 (VH2/VL3) (SEQ ID NO.:9).

Figure 4. A) Nucleotide sequence of anti-CD3 (VH3/VL1) (SEQ ID NO.:10) B) Amino acid sequence of anti-CD3 (VH3/VL1) (SEQ ID NO.:11) C) Nucleotide sequence of

anti-CD3 (VH3/VL2) (SEQ ID NO.:12) D) Amino acid sequence of anti-CD3 (VH3/VL2) (SEQ ID NO.:13) E) Nucleotide sequence of anti-CD3 (VH3/VL3) (SEQ ID NO.:14) F) Amino acid sequence of anti-CD3 (VH3/VL3) (SEQ ID NO.:15).

Figure 5. A) Nucleotide sequence of anti-CD3 (VH5/VL1) (SEQ ID NO.:16) B) Amino acid sequence of anti-CD3 (VH5/VL1) (SEQ ID NO.:17) C) Nucleotide sequence of anti-CD3 (VH5/VL2) (SEQ ID NO.:18) D) Amino acid sequence of anti-CD3 (VH5xVL2) (SEQ ID NO.:19) E) Nucleotide sequence of anti-CD3 (VH5/VL3) (SEQ ID NO.:20) F) Amino acid sequence of anti-CD3 (VH5/VL3) (SEQ ID NO.:21).

Figure 6. A) Nucleotide sequence of anti-CD3 (VH7/VL1) (SEQ ID NO.:22) B) Amino acid sequence of anti-CD3 (VH7xVL1) (SEQ ID NO.:23) C) Nucleotide sequence of anti-CD3 (VH7/VL2) (SEQ ID NO.:24) D) Amino acid sequence of anti-CD3 (VH7xVL2) (SEQ ID NO.:25) E) Nucleotide sequence of anti-CD3 (VH7/VL3) (SEQ ID NO.:26) F) Amino acid sequence of anti-CD3 (VH7/VL3) (SEQ ID NO.:27).

Figure 7. Binding of bispecific anti-CD19 constructs with different deimmunized anti-CD3 parts: the anti-CD3 (VH2/VL1) (SEQ ID NO.:178), anti-CD3 (VH2/VL2) (SEQ ID NO.:180), anti-CD3 (VH2/VL3) (SEQ ID NO.:182), anti-CD3 (VH3/VL1) (SEQ ID NO.:184), anti-CD3 (VH3/VL2) (SEQ ID NO.:186), anti-CD3 (VH3/VL3) (SEQ ID NO.:188), anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VK2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198), anti-CD3 (VH7/VL3) (SEQ ID NO.:200) A) CD3 and B) CD19. Binding was measured by a FACS-based assay using CD3 enriched PBMCs (A) or CD19-positive NALM-cells (B). CD3 and a secondary FITC labeled anti-mouse Ig antibody was used as a negative control in (A) and CD19 and a secondary FITC labeled anti-mouse Ig antibody was used as a negative control in (B). Constructs anti-CD19xanti-CD3 and anti-EpCAM (M79)xanti-CD3 were used as controls. MFI indicates mean fluorescence intensity.

Figure 8: A representative elution pattern of a deimmunized variant of anti CD19 x anti CD3 protein fraction from a HCIC column at 280 nm. The bottom line showing a major step at 700 ml indicates the theoretical gradient of the elution buffer containing 20 mM acetate, pH3.5. High adsorption at 280 nm was due to non-bound protein in

the column flow-through. The arrow at 810,98 ml indicates the eluted deimmunized anti-CD3 fraction.

Figure 9: A representative elution pattern of a deimmunized variant of anti CD19 x anti CD3 protein fraction from a Ni-Chelating His Trap® column at 280 nm. The bottom line showing a first step at 85 ml and a second major step at 90 ml indicates the theoretical gradient of the elution buffer (dotted line). The arrow at 93,16 ml indicates the protein fraction containing the antiCD19 x antiCD3 construct.

Figure 10: A representative protein elution pattern from a Sephadex S200 gelfiltration column. Fractions were collected from 0-130 ml retention time. The protein peak at 80.44 ml corresponds to a MW of ca. 52 kD and contains the deimmunized antiCD19 x antiCD3 construct.

Figure 11: A) SDS-PAGE analysis of deimmunized variants of anti CD19 x anti CD3 protein fractions. Lane M: Molecular weight marker Lane 1: HCIC flowthrough; lane 2: cell culture supernatant; lane 3: HCIC eluate; lane 4: IMAC flowthrough; lane 5: IMAC wash; lane 6: IMAC eluate; lane 7: gel filtration eluate;
B) Western blot analysis of purified deimmunized variants of anti CD19 x anti CD3 protein fractions. Western blot analysis of purified bispecific protein was performed with antibodies directed against the His-Tag (PentaHis, Qiagen) and goat anti mouse Ig labeled with alkaline phosphatase. Lane M: Molecular weight marker Lane 1: HCIC flow through; lane 2: cell culture supernatant; lane 3: HCIC eluate; lane 4: IMAC flow through; lane 5: IMAC wash; lane 6: IMAC eluate; lane 7: gel filtration eluate.

Figure 12. Binding of the purified bispecific anti-CD19 constructs with different deimmunized anti-CD3 parts anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) to A) CD3 and B) CD19 compared to the wild-type anti CD19xanti CD3 construct. Binding was measured by a FACS-based assay using CD3 enriched PBMCs (A) or CD19-positive NALM-cells (B). A secondary antibody with CD3 positive cells was used as a negative control in (A) and a secondary antibody with CD19 positive cells was used as a negative control in (B). Constructs anti-CD19xanti-CD3 and anti-EpCAM (M79)xanti-CD3 were used as controls. Assay

was carried out with concentrations of 1 µg/ml and 5 µg/ml. MFI indicates mean fluorescence intensity.

Figure 13. Cytotoxicity assay of bispecific anti-CD19 constructs with different deimmunized anti-CD3 parts anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VK3) (SEQ ID NO.:200) compared to control.

Figure 14. Sequence alignment of variable heavy region of the non-deimmunized CD3 antibody, VH5 (SEQ ID NO.:74), VH7 (SEQ ID NO.:76), VH2 (SEQ ID NO.:70) and VH3 (SEQ ID NO.:72). Framework region 1 (FR1), complementarity determining region 1 (CDR1), Framework region 1 (FR1), complementarity determining region 2 (CDR2), Framework region 3 (FR3), complementarity determining region 3 (CDR3) and Framework region 4 (FR4) have been depicted. The sequence LAR and VKK in FR1, the sequence ASGYTF and ASGYTA at the transition of framework 1 region to CDR1 region and the sequence LTTDK, ITTDK and MTTDT at FR3 and the sequence MQLS, MELS and LQMN at FR3 have been boxed. Alignment was carried out using the AlingnX program of Vector NTI Advance (Informax, Inc., USA).

Figure 15. Binding analysis of bispecific anti EpCAM constructs with different deimmunized anti-CD3 parts: anti-CD3 (VH5/VL2)x5-10 (SEQ ID NO.:37) (A), deimmunized anti-CD3 (VH5/VL2)x4-7 (SEQ ID NO.:33), (B) deimmunized anti-CD3 (VH5/VL2)x3-1 (SEQ ID NO.:31) (C), deimmunized anti-CD3 (VH5/VL2)x4-7 (VL-VH) (SEQ ID NO.:35) (D) and deimmunized anti-CD3 (VH5/VL2)x5-10 (VL-VH) (SEQ ID NO.:39) (E) in CD3-positive Jurkat and EpCAM-positive Kato III cells with a FACS-based assay. A shift to the right shows binding. In Jurkat cells the dotted line indicates the shift of the negative control (only secondary antibody), dashed line shows the binding of an anti-EpCAM-anti-CD3 control antibody, the bold line shows the bispecific construct of interest. In the binding assay using EpCAM-positive Kato III-cells instead of monoclonal antibody to CD3 a monoclonal antibody to EpCAM was used as a positive control.

Figure 16. Binding analysis of bispecific anti EpCAM constructs with different deimmunized anti-CD3 parts: 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49) (A) and 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63) (B) in CD3-positive Jurkat cells and in EpCAM-positive Kato cells with a FACS based assay. A shift to the right shows binding.

Figure 17. Cytotoxicity assay of EpCAM constructs with deimmunized anti-CD3 parts (di anti-CD3) at N-terminal position anti-CD3 (VH5/VL2)x3-1 (SEQ ID NO.:31), anti-CD3 (VH5/VL2)x-5-10 (SEQ ID NO.:37) and anti-CD3 (VH5/VL2)x4-7 (SEQ ID NO.:33) compared to the corresponding non-deimmunized constructs. CB15 T cell clone and CHO-EpCAM cells were used in an E:T ratio of 5:1. CHO-EpCAM cell were stained with PKH26 dye and the cells were counted after bispecific single chain antibody incubation with FACS analysis.

Figure 18. Cytotoxicity assay of EpCAM constructs with deimmunized anti-CD3 parts at the C-terminal position 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49) and 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63) compared to the corresponding non-deimmunized wild-type constructs. Cytotoxicity assay was carried out identically to Figure 17.

The following Examples illustrate the invention:

In the following examples a number of single chain anti-human CD3 antibodies have been engineered to show reduced immunogenicity in man. The different deimmunized anti-human CD3 antibodies comprise 12 combinations of 4 different VH (VH2 (SEQ ID NO.:69, 70), VH3 (SEQ ID NO.:71, 72), VH5 (SEQ ID NO.:73, 74) and VH7 (SEQ ID NO.:75, 76)) and 3 different VL (VL1 (SEQ ID NO.:77, 78), VL2 (SEQ ID NO.:79, 80) and VL3 (SEQ ID NO.:81, 82)) regions joined together. The amino acid and nucleic acid sequences of the above-mentioned VH and VL regions are shown in Figures 3-6. Illustratively, the deimmunized anti-CD3 single chain antibodies were combined with an anti-CD19 single chain antibody or with an anti-EpCAM single chain antibody in order to form a bispecific product.

Example 1. Cloning and expression of deimmunized anti-CD3 constructs

1.1.Transfer of cDNA encoding single chain antibody

The DNA encoding the anti-CD3 single-chain antibody, which was deimmunized, is referred herein as the anti-CD3 cassette. This anti-CD3 cassette consists of a SGGGGS linker (SEQ ID NO.:176), the anti-CD3 VH region (SEQ ID NO.:110), a 14 amino acid GS linker (VEGGSGGSGGSGGSGGVD linker (SEQ ID NO.:68)), and the anti-CD3 VL chains region (SEQ ID NO.:112) followed by 6 histidine residues. The afore-mentioned DNA was cloned into the vector p-PCR-Script-Amp SK(+) (Stratagene) at the Srf1 site. The DNA and amino acid sequence of the anti-CD3 cassette is shown in SEQ ID NO.:1, SEQ ID NO.:2 and Figure 1.

1.2 Computer analysis of sequences for immunogenic T cell epitopes and design of deimmunized single chain antibody sequences

The amino acid sequence of the anti-CD3 cassette (SEQ ID NO.:2) was analyzed by peptide threading program to identify potential T cell epitopes with the method as described in WO 98/52976. SEQ ID NO.3 shows the deimmunized linker sequence and SEQ ID NO.:68 the original linker sequence.

1.3 Construction of deimmunized single chain antibody sequences

The deimmunized versions of the anti-CD3 cassette were constructed by the method of overlapping PCR recombination. The anti-CD3 cassette (SEQ ID NO.:1, 2) in pPCR-S-Amp SK+ was used as the template for mutagenesis to the required deimmunized sequences. Sets of mutagenic primer pairs were synthezised encompassing the regions to be altered. The deimmunized sequences produced, including 4 different VH and 3 different VL regions, were cloned as Not1 to Hind111 fragments into the vector pPCR-S-Amp SK+ and the entire DNA sequence was confirmed to be correct. The 4 different VH and 3 different VK regions were joined in all combinations (a total of 12), either by PCR or using a unique BstE11 site introduced at the 3' end of the VH region. The entire DNA sequence of each combination was confirmed to be correct. The different deimmunized VH regions (SEQ ID NO.:70, 72, 74 and 76) and VL regions (SEQ ID NO.:78, 80 and 82) with the corresponding original non-deimmunized sequences (VH:SEQ ID NO.:110; VL:SEQ ID NO.:112) of the anti-CD3 constructs are summarized in Table 9.

Table 9. SEQ ID Nos. of deimmunized VH and VL regions

	SEQ ID NO.:		SEQ ID NO.: CDR1		SEQ ID NO.: CDR2		SEQ ID NO.: CDR3	
	Nucleic acid	Amino acid	Nucleic acid	Amino acid	Nucleic acid	Amino acid	Nucleic acid	Amino acid
Deimmunized VH2	69	70	85	86	93	94	95	96
Deimmunized VH3	71	72	85	86	93	94	95	96
Deimmunized VH5	73	74	87	88	91	92	95	96
Deimmunized VH7	75	76	87	88	89	90	95	96
VH of the non-deimmunized CD3	109	110	83	84	89	90	95	96
VH of the non-deimmunized CD3 with Cys→Ser Mutation	105	106	83	84	89	90	107	108
Deimmunized VL1	77	78	99	100	101	102	103	104
Deimmunized VL2	79	80	99	100	101	102	103	104
Deimmunized VL3	81	82	97	98	101	102	103	104
VL of the non-deimmunized CD3	111	112	97	98	101	102	103	104

1.4 Transfer of deimmunized single chain antibody genes into expression vector

The deimmunized anti-CD3 cassettes were excised from pPCR–S-Amp-SK+ with BspE1 and Sal1 and cloned into the expression vector pEF comprising VL_{CD19}-VH_{CD19}-VH_{CD3}-VL_{CD3}. The CD3 part of the pEF-DHFR vector was replaced with each of the deimmunized anti-CD3 cassettes from the BspE1 site to the Sal1 site resulting in the following 12 constructs:

pEF anti-CD19xanti-CD3 (VH2/VL1) (SEQ ID NOs. 177, 178)
pEF anti-CD19xanti-CD3 (VH2/VL2) (SEQ ID NOs. 179, 180)
pEF anti-CD19xanti-CD3 (VH2/VL3) (SEQ ID NOs. 181, 182)
pEF anti-CD19xanti-CD3 (VH3/VL1) (SEQ ID NOs. 183, 184)
pEF anti-CD19xanti-CD3 (VH3/VL2) (SEQ ID NOs. 185, 186)
pEF anti-CD19xanti-CD3 (VH3/VL3) (SEQ ID NOs. 187, 188)
pEF anti-CD19xanti-CD3 (VH5/VL1) (SEQ ID NOs. 189, 190)

pEF anti-CD19xanti-CD3 (VH5/VL2) (SEQ ID NOs. 191, 192)
pEF anti-CD19xanti-CD3 (VH5/VL3) (SEQ ID NOs: 193, 194)
pEF anti-CD19xanti-CD3 (VH7/VL1) (SEQ ID NOs. 195, 196)
pEF anti-CD19xanti-CD3 (VH7/VL1) (SEQ ID NOs. 197, 198)
pEF anti-CD19xanti-CD3 (VH7/VL3) (SEQ ID NOs. 199, 200).

The constructs further comprises a murine IgG heavy chain leader in order to enable the secretion ot the protein. The DNA sequences of the deimmunized anti-CD3 cassettes in the expression vector were confirmed using the sequencing primers (SEQ ID No.: 28 and 29). The DNA and amino acid sequences of the 12 deimmunized anti-CD3 cassettes in the pEF vector from the BspE1 site to the Sal1 site are shown in SEQ ID NO.:s 177-200.

1.5 Production of antibody constructs

After transformation of the vector into E. coli K12, transfection-grade DNAs of the different expression vectors were prepared. Secreted proteins were produced in CHO-dhfr- cells. For transient production the cell culture supernatants were harvested 2 days after transfection, for the generation of stable transfected cells, cells were put in selection medium two days after transfection. After five passages, stable pools were obtained. Subsequently, single clones were identified in limiting dilutions. To facilitate the purification process, the cells were adapted to serum-free medium. Antibody constructs were purified from about 1 liter of supernatant.
The production levels were tested in ELISA. No major differences in the secreted antibody levels were observed between different constructs comprising anti-CD19 and deimmunized anti-CD3 constructs.

Example 2: Binding Assays

In order to analyze the binding efficacy of the deimmunized constructs to CD3 and CD19 a FACS-based assay was performed. Initially, crude supernatants were tested for binding on CD3-enriched PBMCs or CD19-positive NALM-6 cells. Cells were incubated with non-diluted supernatants for 30 minutes at 8 °C. Upon two wash steps the cells were labeled with an anti-His antibody (Qiagen) under the same conditions. After additional wash steps binding of the constructs was detected with a FITC-conjugated sheep anti-mouse antibody (Sigma). Cells were analyzed with a FACS Calibur cytometer (B&D). As controls supernatants of anti CD19xanti CD3 and GFP-transfected cells were included. CD3 and a secondary antibody was used as a

negative control and it showed a mean fluorescence intensity (MFI) of ca. 3.5. The anti-CD19xanti-CD3 constructs comprising anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) had a MFI of at least 90, thus binding about 25 times more strongly. The positive control, which was a non-deimmunized anti-CD19xanti-CD3 construct reached a MFI of around 60 showing that the deimmunized constructs comprising anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) bound CD3 with extremely high efficacy. In a second experiment, the following constructs comprising anti-CD19 and anti CD3: anti-CD3 (VH2/VL1) (SEQ ID NO.:178), anti-CD3 (VH2/VL2) (SEQ ID NO.:180), anti-CD3 (VH2/VL3) (SEQ ID NO.:182, anti-CD3 (VH3/VL1) (SEQ ID NO.:184), anti-CD3 (VH3/VL2) (SEQ ID NO.:186) and anti-CD3 (VH3/VL3) (SEQ ID NO.:188), showed similar binding as the negative control (MFI ca. 6).

The FACS-based binding assay was also carried out for CD19. In this experiment CD19 and a secondary antibody was as a negative control. In this experiment, all assayed constructs achieved a MFI of at least 80 while the MFI of the negative control was ca. 3.

Thus, the constructs comprising anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) turned out to bind as well CD3 and CD19 as the non-modified anti CD19xanti CD3 (SEQ ID NO.:204). However, the constructs anti-CD3 (VH2/VL1) (SEQ ID NO.:178), anti-CD3 (VH2/VL2) (SEQ ID NO.:180), anti-CD3 (VH2/VL3) (SEQ ID NO.:182), anti-CD3 (VH3/VL1) (SEQ ID NO.:184), anti-CD3 (VH3/VL2) (SEQ ID NO.:186), anti-CD3 (VH3/VL3) (SEQ ID NO.:188) had completely lost anti-CD3 binding capacity, while CD19 binding was fully retained (Figure 7).

Thus, it was demonstrated that the deimmunized heavy chains dominated the binding specificity and strength. As a result, the anti-CD3 constructs with VH5 and VH7 groups were purified and analyzed for cytotoxic activity.

Example 3. Expression and purification of the variants showing high binding affinity

The deimmunized anti-CD19xanti-CD3 proteins anti-CD3 (VH5/VLI1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) were expressed in chinese hamster ovary cells (CHO).

In order to purify the bispecific single-chain constructs comprising a deimmunized anti-CD3 part CHO-CD19 cells were grown in roller bottles with HiClone CHO modified DMEM medium (HiQ)® for 7 days before harvest. The cells were removed by centrifugation and the supernatant, containing the expressed protein was stored at –20°C.

Äkta FPLC System® (Pharmacia) and Unicorn Software® were used for chromatography. All chemicals were of research grade and purchased from Sigma (Deisenhofen) or Merck (Darmstadt).

Hydrophobic charge induction chromatography was performed on MEP Hypercel® medium loaded to a XK16/60 column (Pharmacia) that was equilibrated with buffer A1 (20 mM Tris pH 7.2). 500ml of cell culture supernatant were applied to the column (10 ml) with a flow rate of 3 ml/min. Unbound sample was washed out with buffer A1 and the bound protein was eluted with 100% buffer B1 (20 mM acetate pH 3.5). Eluted protein fractions were pooled for further purification.

IMAC was performed, using a HisTrap® column (Pharmacia) that was loaded with $NiSO_4$ according to the manufacturers protocol. The column was equilibrated with buffer A2 (20 mM NaP pH 7.5, 0.4 M NaCl) and the sample was diluted 2:1 with buffer A2 to obtain a pH of 7. The sample was applied to the column (2 ml) with a flow rate of 1 ml/min and the column was washed with buffer A2 to remove unbound sample. Bound protein was eluted using a 2 step gradient of buffer B2 (20 mM NaP pH 7.5, 0.4 M NaCl, 0.5 M Imidazol) Step 1: 20% buffer B2 in 10 column volumes; Step 2: 100% buffer B2 in 10 column volumes. Eluted protein fractions were pooled for further purification.

Gel filtration chromatography was performed on a Sephadex S200 HiPrep® column (Pharmacia) equilibrated with PBS (Gibco). Eluted protein samples (flow rate 1ml/min) were subjected to SDS-Page and Western Blot for detection (Figure 11).

The column was previously calibrated for molecular weight determination (molecular weight marker kit, Sigma MW GF-200).

The deimmunized variants of anti CD19 x anti CD3 protein were isolated in a three step purification process including hydrophobic charge induction chromatography (HCIC) (Figure 8), immobilized metal affinity chromatography (IMAC) (Figure 9) and gel filtration (Figure 10). The bispecific constructhad a molecular weight of 52 kDa under native conditions as determined by gelfiltration in PBS.

The purified bispecific protein was analyzed with SDS PAGE under reducing conditions using precast 4-12% Bis Tris gels (Invitrogen). Sample preparation and application were according to the manufacturers protocol. The molecular weight was determined with MultiMark® protein standard (Invitrogen). The gel was stained with colloidal Coomassie (Invitrogen protocol). The purity of the isolated protein was >95% (Figure 11a) and the molecule has a size of 52 kD.

Furthermore, the deimmunized variants of anti CD19 x anti CD3 protein were specifically detected by Western Blot. Western Blot was performed with an Optitran BA-S83® membrane and the Invitrogen Blot Module® according to the manufacturers protocol. The antibodies used were Penta His (Quiagen) and Goat-anti-Mouse-Ig labeled with alkaline phophatase (AP) (Sigma), the staining solution was BCIP/NBT liquid (Sigma). The main signal was shown to correspond to the main band in the SDS PAGE at 52kD (Figure 11b).

Protein concentrations were determined using protein assay dye (MicroBCA®, Pierce) and IgG (Biorad) as standard protein. A summary of the final yields of purified protein variants is given in Table 10 showing the high productivity of all the constructs and very good yield of construct with anti CD3 (VH5/VL1) (SEQ ID NO.:190) of 924.8 µg.

Table 10. Protein yields of the deimmunized anti-CD19-anti-CD3 constructs

Deimmunized CD3 construct	Yield [µg/supernatant]
CD19xanti CD3 (VH5/ VL1)(SEQ ID NO.:190)	924.8
CD19xanti CD3 (VH5/ VL2)(SEQ ID NO.:192)	446.7
CD19xanti CD3 (VH5/ VL3)(SEQ ID NO.:194)	218.4
CD19xanti CD3(VH7/ VL1)(SEQ ID NO.:196)	268.5
CD19xanti CD3(VH7/VL2)(SEQ ID NO.:198)	553.4
CD19xanti CD3(VH7/VL3) (SEQ ID NO.:200)	477.3

The productivity of the CD19xanti CD3 (VH5/ VL2) and CD19xanti CD3(VH7/VL2) constructs was compared with the corresponding non-deimmunized constructs. The results are shown in Table 11.

Table 11. Yields of the deimmunized bispecific construct compared to the corresponding non-deimmunized construct

Construct	Yield (µg/l)
CD19xanti-CD3	62
CD19xantiCD3(VH5/VL2)	204
CD19xantiCD3(VH7/VL2)	310

Table 11 clearly demonstrates that the bispecific constructs comprising deimmunized CD3 binding domain have much higher (at least three fold) productivity than the corresponding non-deimmunized construct.

Example 4. FACS based binding assays of the anti-CD3 constructs

Binding of selected purified antibody constructs comprising anti-CD19 and anti-CD3 was detected as described above in Example 2 at various concentrations. In the CD3 binding assay, the negative control secondary antibody (anti-His, FITC-conjugated), which was incubated with CD3 positive cells, showed a MFI of about 2.5 and the positive control deimmunized antiCD19xanti-CD3 bispecific single chain antibody of about 70 at 1 µg/ml concentration and 50 at 5 µg/ml concentration (Figure 12A). At the concentration of 1 µg/ml, the anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) deimmunized bispecific antibodies showed MFI values of 10-20; anti-CD3 (VH5/VL1) (SEQ ID NO.:190) having the highest (20). At 5 µg/ml anti-CD3 (VH7/VL2) (SEQ ID NO.:198) reached a MFI of 25, while anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL3) (SEQ ID NO.:200) and anti-CD3 (VH5/VL1) (SEQ ID NO.:190) had an MFI of at least 40 thus, showing the same binding efficacy than the non-deimmunized positive control. At a concentration of 5 µg/ml the strongly binding constructs with deimmunized anti CD3 part VH5/VL1 (SEQ ID NO.:190), VH7/VL1 (SEQ ID NO.:196), VH7/VL2 (SEQ ID NO.:198), VH7/VL3 (SEQ ID NO.:200) bound to CD3 as well as the non-deimmunized anti CD19xanti CD3 (SEQ ID NO.:204).

All the antibody constructs bound to CD19 with a high efficacy, which was at about 200 MFI, while non-deimmunized anti-CD19xanti-CD3 construct (SEQ ID NO.:204)

showed 80 MFI. No differences were observed for CD19 binding at the tested concentrations for the different constructs (Figure 12B).

Example 5. Cytotoxicity Assays

anti CD19xanti CD3 mediates T cell dependent cytotoxicity to CD19-positive target cells. This was analyzed in vitro for the determination of the biological potency of anti CD19xanti CD3.

For this purposes fluorescence labeled CD19-positive NALM-6 target cells were incubated with isolated PBMC of random donors or CB15 T-cells (standardized T-cell line) as effector cells in the presence of anti CD19xanti CD3. After incubation for 4 h at 37 °C in a humidified incubator, the release of the fluorescent dye from the target cells into the supernatant is determined in a spectrofluorimeter. Target cells incubated without anti CD19xanti CD3 and target cells totally lysed by the addition of saponin at the end of the incubation serve as negative and positive controls, respectively. The specific cytotoxicity mediated at a certain anti CD19xanti CD3 concentration can be calculated with the following formula:

$$\text{Specific Cytotoxicity [\%]} = \frac{\text{RFU (Sample)} - \text{Mean RFU (control)}}{\text{Mean RFU (total lysis)} - \text{Mean RFU (control)}} \times 100$$

The dose response was analyzed from 0.4 pg/ml anti CD19xanti CD3 to 100 ng/ml anti CD19xanti CD3 to specify the EC50 value. Although the EC50 value describes the biological potency of anti CD19xanti CD3, the absolute value will vary significantly depending on the source of the effector cells. Thus a relative potency is calculated in comparison to an anti CD19xanti CD3 reference material based on the following formula:

$$\text{Relative Potency} = \frac{\text{EC50 Sample}}{\text{EC50 Reference}}$$

The cytotoxic activities of the constructs comprising anti-CD19 and deimmunized anti-CD3 are shown in Figure 13. Purified non-deimmunized anti-CD19xanti CD3 was used as control. The EC50 values of the deimmunized constructs were at a range of 21.9-81.6 pg/ml while the EC50 value of the non-deimmunized anti-CD19xanti-CD3 construct was 22.7 pg/ml. Thus, all deimmunized constructs revealed EC 50 values comparable to the non-deimmunized molecule.

Example 6. T-cell proliferation assay

Twenty healthy donors were selected for screening in T cell assays based on HLA-DR typing (Table 12). This enables the screening of peptides in the T cell assay against greater than 80% of DR alleles expressed in the world population.

Table 12: HLA DR haplotypes of 20 healthy donors used to test the immunogenicity of peptides obtained from deimmunized and non-deimmunized anti-CD3 scAb.

	HLA DR Allotype
1	DRB1*07, DRB1*15, DRB4*01, DRB5
2	DRB1*03, DRB1*04, DRB3, DRB4*01
3	DRB1*04, DRB1*07 and DRB4*01
4	DRB1*07, DRB1*11, DRB4*01
5	DRB1*04, DRB1*07, DRB4*01
6	DRB1*01, DRB1*04, DRB4*01
7	DRB1*03, DRB1*07, DRB3, DRB4*01
8	DRB1*07, DRB1*11, DRB3, DRB4*01
9	DRB1*12. DRB1*15, DRB3, DRB5
10	DRB1*01, DRB1*09, DRB4*01
11	DRB1*03, DRB1*15, DRB3, DRB5
12	DRB1*10, DRB1*13, DRB3
13	DRB1*03, DRB1*15, DRB3, DRB5
14	DRB1*04, DRb1*15, DRB4*01, DRB5
15	DRB1*04, DRB1*13, DRB3, DRB4*01
16	DRB1*01, DRB1*13, DRB3
17	DRB1*01, DRB1*04, DRB4*01
18	DRB1*07, DRB1*13, DRB3, DRB4*01
19	DRB1*07, DRB1*16, DRB4*01, DRB5
20	DRB1*04, DRB1*15, DRB4*01, DRB5

6.1 T-Cell Proliferation Assay

Peptides were obtained from Pepscan (Netherlands) at a purity of greater than 90%. Peripheral blood mononuclear cells (PBMC) from the 20 selected healthy donors (Table 12) were used to screen individual peptides in triplicate wells at 1 and 5 μM. Two positive control peptides (C32 and C49) and keyhole limpet hemocyanin (KLH) were included in the assay. After 7 days incubation of cells and peptides, an 18 hour pulse with 3H-thymidine at 1μCi/well was used to assess T cell proliferation. These data are expressed as stimulation index where:

Stimulation Index = CPM of test peptide / CPM of untreated control

A T cell epitope is defined as a peptide giving a stimulation index (SI) greater than 2.

The results from two independent runs indicated that 5 of the 22 MHC binding peptides in the non-deimmunized anti-CD3 sequence had the capacity to induce human T cell proliferation (SI>2). In contrast, none of the corresponding deimmunized molecules induced T cell proliferation. Table 13 summarizes the T cell proliferation assay results showing Mean SI values of 2 independent runs.

The data also showed a concentration dependent effect whereby each of the non-deimmunized binding molecules showed SI's > 2 in only one of the two concentrations (1μm or 5μm) used. The difference in response at different concentrations is explained by the fact that individual peptides will have optimum concentrations at which they induced T cell proliferation. If this concentration is exceeded, then proliferation can drop off (high peptide concentrations can have an inhibitory effect on T cell proliferation). This explains why, in some instances, proliferation is seen at the lower concentration and not at the higher. From experience, T cell proliferation will be observed at one or two of the peptide concentrations used if a peptide contains a T cell epitope. These data demonstrated that deimmunization had successfully removed T cell epitopes from anti CD3 (VH5/VL2) (SEQ ID NO.:19) and anti CD3 (VH7/VL2) (SEQ ID NO.:25). The fact that about 75% of MHC binding peptides from the non-deimmunized anti-CD3 sequence did not induce T cell proliferation can be explained either by tolerance of the human immune system to these peptides or an inability of the human T cell repertoire to recognise these particular peptides.

Table 13: Summary of data comparing positive (SI>2) mouse peptides and corresponding deimmunized peptides.

Peptide Region	Allotype	Concentration (µM)	*Non-deimmunized Anti-CD3* Mean SI	*Deimmunized Anti-CD3* Mean SI
6-20	5	5	2.51	0.77
74-86	5	1	2.52	0.97
				0.96
90-102	5	5	2.21	0.56
				1.38
90-102	6	5	2.24	0.90
				0.82
90-102	11	5	2.23	0.83
				0.78
162-174	5	1	3.82	0.59
216-230	10	1	2.12	1.03

Example 7. Homology alignment of anti-CD3 (VH5), anti-CD3 (VH7), anti-CD3 (VH2) and anti-CD3 (VH3) with the non-deimmunized anti-CD3 VH

The variable heavy region of the non-deimmunized CD3 antibody, VH5 (SEQ ID NO.:74), VH7 (SEQ ID NO.:76), VH2 (SEQ ID NO.:70) and VH3 (SEQ ID NO.:72) were aligned using the AlingnX program of Vector NTI Advance (Informax, Inc., USA). The Clustal W algorithm used is described in Nucleic Acid Research, 22 (22): 4673-4860, 1994. The alignment is shown in Figure 14. From the alignment can be seen that the variable regions VH5 and VH7, which show surprisingly good binding have the sequence ASGYTF at the transition region of framework 1 to CDR1. Furthermore, the VH regions showing no binding (VH2 (SEQ ID NO:70) and VH3 (SEQ ID NO.:72)) comprise the sequence ASGYTA at the transition of framework 1 to CDR1. Thus, for obtaining a construct having reduced propensity to generate T cell epitopes and binding to CD3, the construct has to comprise the sequence ASGYTF at the transition of framework 1 to CDR1. Surprisingly, the variable heavy regions binding to CD3 and showing reduced propensity to generate T cell epitopes comprising the above-mentioned sequence ASGYTF show good binding.

Example 8. Cloning of constructs comprising deimmunized anti-CD3 and anti-EpCAM

In order to demonstrate that the deimmunized anti-CD3 polypeptide of the invention can be a part of a functional construct with other targets, a number of bispecific constructs comprising deimmunized anti-CD3 (VH5/VL2) (SEQ ID NO.:19) and different anti-EpCAM single chain antibodies (3-1 (SEQ ID NO.:137, 139), 3-5 (SEQ ID NO.:141, 143), 4-1 (SEQ ID NO.:145, 147), 4-7 (SEQ ID NO.:149, 151), 5-10 (SEQ ID NO.:133, 135)) were generated.

8.1 Cloning of C-terminal EpCAM binders comprising deimmunized anti-CD3 part (SEQ ID Nos.: 30, 31, 32, 33, 34, 35, 36, 37, 38 and 39)

8.1.1 Amplification of the deimmunized anti-CD3 from the anti-CD19xanti CD3 (VH5/VL2) construct (SEQ ID NO.:192)

The N-terminal deimmunized anti CD3(VH5/VL2) was obtained by PCR using the deimmunized (CD19 x anti-CD3 (VH5/VL2) (SEQ ID NO:192) as template and the following primers (DI CD3 5-2 VH BsrGI AGGTGTACACTCCGACGTCCAACTGGTGCAGTCAG (SEQ ID NO.:40), DI CD3 5-2 VL BspEI AATCCGGATTTGATCTCCACCTTGGTCCCG (SEQ ID NO.:41).

8.1.2. Cloning and expression of the deimmunized anti-CD3xanti-EpCAM deimmunized constructs in VH_{CD3}-VL_{CD3} x VH_{EpCAM}-VL_{EpCAM} orientation

The above mentioned PCR product containing the deimmunized anti-CD3 was cleaved with the restriction enzymes BsrG1 and BspE1 and subsequently cloned into the bluescript KS vector (Stratagene, La Jolla, CA), containing the amino acid sequence of an eukaryotic secretory signal (leader peptide) as a EcoRI/BsrGI-fragment. After cleavage of this construct with EcoRI and BspEI the resulting DNA fragment comprising the respective anti-CD3 scFv with the leader peptide was cloned into a EcoRI/BspEI cleaved plasmid containing the anti EpCAM scFv 3-1, 4-7, or 5-10 in C-terminal position in pEF-DHFR- vector. After confirmation of the sequence coding for the bispecific single chain by sequencing (Sequiserve, Vaterstetten) the plasmid was transfected into DHFR deficient CHO cells for eukaryotic expression. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described in Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566).

8.1.3. Cloning and expression of the deimmunized anti-CD3xanti-EpCAM constructs in VH_{CD3}-VL_{CD3} x VL_{EpCAM}-VH_{EpCAM} orientation

Anti-EpCAM 4-7 in VL-VH orientation containing the 15 amino acid standard linker (SEQ ID NO.:168) was obtained by PCR. The 4-7 VH region and the 4-7 VL region

were separately amplified by the following primers (4-7 VL: 4-7 VL BspEI FOR CTGAAATCCGGAGGTGGTGGATCCGAGCTCGTGATGACCCAGACTCC (SEQ ID NO.:117), 4-7 VL GS15 REV GGAGCCGCCGCCGCCAGAACCACCACCACCTTTGATCTCAAGCTTGGTCCCC (SEQ ID NO.:118); 4-7 VH: 4-7 VH GS15 FOR GGCGGCGGCGGCTCCGGTGGTGGTGGTTCTGAGGTGCAGCTGCTCGAGCAG (SEQ ID NO.:42), 4-7 VH SalI REV TTTTAAGTCGACCTAATGATGATGATGATGATGATGTGAGGAGACGGTGACCGTGG (SEQ ID NO.:43)). Overlapping complementary sequences introduced into the PCR products were used to form the coding sequence of a 15-amino acid $(G_4S_1)3$ (single-letter amino acid code) linker (standard linker) (SEQ ID NO.:168) during the subsequent fusion PCR. This amplification step was performed with the primer pair 4-7 VL BspEI FOR and 4-7 VH SalI REV (SEQ ID Ns. 42 and 43).

Anti-EpCAM 5-10 in VL-VH orientation containing the 15 amino acid standard $((G_4S_1)3)$ linker was obtained by PCR. The 5-10 VH region and the 5-10 VL region were separately amplified by the following primers (5-10 VL: 5-10 VL BspEI FOR CTGAAATCCGGAGGTGGTGGATCCGAGCTCGTGATGACACAGTCTCCAT (SEQ ID NO.:44), 5-10 VL GS15 REV GGAGCCGCCGCCGCCAGAACCACCACCACCTTTGATCTCAAGCTTGGTCCCAG; (SEQ ID NO.:45) 5-10 VH: 5-10 VH GS15 FOR GGCGGCGGCGGCTCCGGTGGTGGTGGTTCTGAGGTGCAGCTGCTCGAGC (SEQ ID NO.:46), 5-10 VH SalI REV TTTTAAGTCGACCTAATGATGATGATGATGATGTGAGGAGACGGTGACCGTGG (SEQ ID NO.:47). Overlapping complementary sequences introduced into the PCR products were used to form the coding sequence of a 15-amino acid $(G_4S_1)_3$ (single-letter amino acid code) linker (standard linker) (SEQ ID NO.:168) during the subsequent fusion PCR. This amplification step was performed with the primer pair 5-10 VL BspEI FOR and 5-10 VH SalI REV.

The PCR products 5-10 VL-VH and 4-7 VL-VH) were cloned into the pEF-DHFR vector comprising anti-CD3 construct (VH5/VL2). After confirmation of the sequence coding for the bispecific single chain by sequencing the plasmid was transfected into DHFR deficient CHO cells for eukaryotic expression. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described in Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566).

8.1.4. Binding of the deimmunized anti-CD3xanti-EpCAM constructs to EpCAM and CD3

Binding of the bispecific single chain molecules with anti-CD3 part in N-terminal orientation to EpCAM and CD3 were confirmed by FACS analyses. For that purpose the EpCAM positive human gastric cancer cell line Kato III (ATCC HTB-103) was used. Binding of the anti-CD3 part was demonstrated on Jurkat cells (ATCC TIB 152).

Cells were cultured according to the recommendations of the supplier and a number of 200000 cells was incubated with 10µg/ml of the construct in 50µl PBS with 2%FCS (fetal calf serum). The binding of the construct was detected with an anti-His antibody (Penta-His Antibody, obtained from Quiagen, Hilden, FRG) at 2µg/ml in PBS with 2%FCS. As a second step R-Phycoerythrin-conjugated affinity purified $F(ab')_2$ derived from goat anti-mouse IgG, diluted 1:100 in 50µl PBS with 2% FCS (Dianova, Hamburg, FRG) was used. The samples were measured on a FACSscan (BD biosciences, Heidelberg, FRG).

Results of FACS analysis are shown in Fig. 15. All constructs comprising deimmunized anti-CD3 part showed stronger binding than the non-deimmunized anti-EpCAM (M79)xanti-CD3 bispecific single-chain antibody on EpCAM positive KatoIII cells.

8.2 Cloning of N-terminal EpCAM binders comprising deimmunized anti-CD3 part

8.2.1 Cloning of the anti-EpCAM x anti-CD3 constructs

8.2.1.1 Cloning of deimmunized 3-1xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:48, 49):

Deimmunized construct 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.: 48) was derived from non-deimmunized construct anti-EpCAM (3-1)xanti-CD3. The VH and VL regions of the anti-EpCAM antibody 3-1 are shown in SEQ ID NO.:137 and 139. The plasmids pEF-DHFR-3-1x anti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.:192) were digested with BspEI and SalI (Biolabs) for the isolation of the vector and the insert anti-CD3 (VH5/VL2), respectively. The BspEI-SalI-digested vector was dephosphorylated and purified on 0.7% agarose gel, whereas the insert was purified on 1.5% agarose gel.

The purified fragment (BspEI-SalI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final 3-1xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:48, 49) was verified by restriction digests and by DNA sequencing of the entire insert.

Cloning of the non-deimmunized 3-1xanti-CD3 construct:

For the cloning of the 3-1xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

The C-terminal 3-1 in VH-VL orientation was obtained by PCR for the construction of non-deimmunized 3-1 x anti-CD3 molecule. Fragments I and II comprising the 3-1 VH-VL in two parts were amplified by PCR using primer pairs me 91a (SEQ ID NO. 53) /me 90 (SEQ ID NO. 52) and me 83 (SEQ ID NO. 50) /me 84 (SEQ ID NO. 51), respectively. Hot Start PCR was done using the Expand High Fidelity System of Roche Diagnostics. 20 cycles (94°C/30 sec; 60°C/1min;72°C/1min) were used for amplification followed by one cycle of 3 min at 72°C.

PCR fragments I and II were subjected to electrophoresis on a 1.5% agarose gel. Fragments were mixed (1 ng of each) and used as a template for the next PCR reaction performed with primer pair me 91a (SEQ ID NO. 53) and me 84 (SEQ ID NO. 51) for amplification of fragment III comprising the entire 3-1. PCR was performed as described above, but with an annealing temperature of 68°C. Fragment III was purified on an agarose gel and digested with BsrGI and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR-anti EpCAM (M79) X anti-CD3 construct. The cloned region was verified by restriction digests and by DNA-sequencing.

Sequences of the Primers used:

Me 83: 5′- GGT TCT GGC GGC GGC GGC TCC GGT GGT GGT GGT TCT GAG GTG CAG CTG CTC GA CAG TCT G -3′ (SEQ ID NO. 50)

Me 84: 5′- GTG CTC CGG AGG AGA CGG TGA CCG TGG TCC CTT GGC CCC AG -3′ (SEQ ID NO. 51)

Me 90: 5′- CCG GAG CCG CCG CCG CCA GAA CCA CCA CCA CCT TTG ATC TCA AGC TTG GTC CC -3′ (SEQ ID NO. 52)

Me 91a: 5′- GGA TTG TAC A CTCC GA GCT CGT CAT GAC CCA GTC TCC ATC TTA TCT TGC TGC -3′ (SEQ ID NO. 53)

8.2.1.2 Cloning of deimmunized 3-5xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:54, 55):

The C-terminal 3-5 in VH-VL orientation was obtained by PCR for the construction of 3-5 xanti-CD3 molecule. The VH and VL regions of the anti-EpCAM antibody 3-5 are shown in SEQ ID NO.:141 and 143. The plasmids pEF-DHFR-3-5xanti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO 192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (3-5) and the vector respectively. The dephosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final 3-5xanti-CD3 (VH5/VL2) (SEQ ID NO.:54) construct was verified by restriction digests.

Cloning of the non-deimmunized 3-5xanti-CD3 construct:

For cloning of the 3-5xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 3-5 in two parts were amplified by PCR according to the conditions described for 3-1xanti-CD3 using primer pairs me 81 (SEQ ID NO. 56) /me 90 (SEQ ID NO. 52) and me 83 (SEQ ID NO. 50) /me 84 (SEQ ID NO. 51) respectively. Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 81 (SEQ ID NO. 56) and me 84 (SEQ ID NO. 51) for amplification of fragment III comprising the entire 3-5. PCR was performed as described above. Fragment III was purified on an agarose gel and digested with BssHII and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFRcloning vector. The cloned region was verified by restriction digests and by DNA-sequencing.

Sequence of the Me81 Primer (Seq ID NO.:56):

Me 81: 5´- GGA TGC GCG CGA GCT CGT GAT GAC CCA GAC TCCA CTC TCC -3´

8.2.1.3 Cloning of the deimmunized 4-1xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:57, 58):

The C-terminal 4-1 in VH-VL orientation was obtained by PCR for the construction of 4-1xanti-CD3 molecule. The VH and VL regions of the anti-EpCAM antibody 4-1 are shown in SEQ ID NO.:145 and 147. The plasmids pEF-DHFR-4-1xanti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.:192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (4-1) and the vector respectively. The dephosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the vector. The final construct 4-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:57) was verified by restriction digests.

Cloning of the non-deimmunized 4-1xanti-CD3 construct:

For cloning of the 4-1xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 4-1 in two parts were amplified by PCR using primer pairs me 91a (SEQ ID NO. 53) /me 90 (SEQ ID NO. 452) and me 83 (SEQ ID NO. 50) /me 84 (SEQ ID NO. 51) with the above-mentioned conditions, respectively.

Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 92a (SEQ ID NO. 59) and me 84 (SEQ ID NO. 51) for amplification of fragment III comprising the entire 4-1. PCR was performed as described above but annealing was performed at 68°C. Fragment III was purified on an agarose gel and digested with BsrGI and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR-anti EpCAM (M79) X anti-CD3 cloning vector construct. The cloned region was verified by restriction digests and by DNA-sequencing.

Sequence of the Me92a primer (SEQ ID NO. 59):

Me 92a: 5´- GGA TTG TAC A CTCC GA GCT CGT GAT GAC ACA GTCTCC ATC CTC C -3´

8.1.2.4 Cloning of the deimmunized 4-7xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:60, 61):

The C-terminal 4-7 in VH-VL orientation was obtained by PCR for the construction of 4-7 xanti-CD3. The VH and VL regions of the anti-EpCAM antibody 4-7 are shown in SEQ ID NO.:149 and 151. The plasmids pEF-DHFR-4-7xanti-CD3 and pEF anti-CD3 VH5/VL2 (SEQ ID NO.:192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (4-7) and the vector respectively. The de-phosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final construct 4-7xanti-CD3 (VH5/VL2) (SEQ ID NO.:60) was verified by restriction digests.

Cloning of the non-deimmunized construct 4-7xanti-CD3:

For cloning of the 4-7xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 4-7 in two parts were amplified by PCR using primer pairs me 81 (SEQ ID NO.:56) /me 90 (SEQ ID NO.:52) and me 83 (SEQ ID NO.:50) /me 84 (SEQ ID NO.:51) with the afore mentioned conditions, respectively.

Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 81 (Seq ID NO.:56) and me 84 (Seq ID NO.:51) for amplification of fragment III comprising the entire 4-7 VH and VL chain. PCR was performed as

described above. Fragment III was purified on an agarose gel and digested with BssHII and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR cloning vector. The cloned region was verified by restriction digests and by DNA-sequencing.

8.1.2.5 Cloning of the deimmunized 5-10x anti-CD3 (VH5/VL2) construct (SEQ ID NO. 62, 63):

The C-terminal 5-10 in VH-VL orientation was obtained by PCR for the construction of 5-10 xanti-CD3 molecule. The VH and VL regions of the anti-EpCAM antibody 5-10 are shown in SEQ ID NO.:133 and 135. The plasmids pEF-DHFR-5-10xanti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.:192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (5-10) and the vector respectively. The dephosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final construct 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO. 62) was verified by restriction digests and by DNA sequencing.

Cloning of the non-deimmunized 5-10xanti-CD3 construct:

For cloning the 5-10xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 5-10 in two parts were amplified by PCR using primer pairs me 92a (SEQ ID NO. 59) /me 90 (SEQ ID NO. 52) and me 83 (SEQ ID NO. 50) /me 84 (SEQ ID NO. 51) with the above mentioned conditions, respectively.

Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 92a SEQ ID NO. 59) and me 84 (SEQ ID NO. 51) for amplification of fragment III comprising the entire 5-10. PCR was performed as described above but annealing was performed at 68°C. Fragment III was purified on an agarose gel and digested with BsrGI and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR-anti EpCAM (M79) x anti-CD3 cloning vector. The cloned region was verified by restriction digests and by DNA-sequencing.

8.2.2 Expression of anti EpCAMxdeimmunized-anti CD3 molecules with anti-EpCAM at the N-terminal position:

CHO-cells lacking DHFR gene were maintained in alpha MEM medium (Life Technologies, cat.no: 32561) supplemented with 10% fetal calf serum(Life

Technologies, heat inactivated at 65°C for 30 minutes) and with HT (Hypoxanthin and Thymidine; Life Technologies). The cells were transfected with pEF-DHFR-3-1xanti-CD3 (VH5/VL2) (SEQ ID NO. 48) and pEF-DHFR-5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:62), using Lipofectamine 2000 kit® (Invitrogen) according to the instructions provided by the Manufacturer. After 48 hrs. selection was performed in selection medium (alpha MEM medium containing heat inactivated 10% dialysed fetal calf serum (Life Technologies). After 3-4 weeks cell culture supernatant was collected and centrifuged at 4°C for 10 minutes at 300g to remove cells and cell debris. The supernatant containing the bispecific antibody was stored at –20°C till further analysis.

8.2.3 Binding assays of bispecific anti-EpCAMxanti CD3 variants:

250000 Jurkat cells (for CD3 binding) and Kato cells (for EpCAM binding) were independently incubated with cell culture supernatants (50µl) containing the bispecific construct (pEF-DHFR-3-1xanti-CD3 (VH5/VL2) (Nr.50, SEQ ID NO. 48) and pEF-DHFR-5-10xanti-CD3 (VH5/VL2) (Nr.54) (SEQ ID NO.:62), respectively) for 45 min. at 4°C. Thereafter, the cells were washed twice in FACS buffer (phosphate-buffered saline containing 1% fetal calf serum (FCS) and 0.05% sodium azide) and incubated with mouse anti-His antibody (Dianova,DIA910) for 60 min. at 4°C. Washing steps were performed as above.

The cells were finally incubated either with goat anti-mouse Ig-FITC-conjugated antibody (BD 550003) or with anti-mouse IgG conjugated with PE (Sigma, P8547). After washing steps, 10000 events were analysed using FACS Calibur (B&D). The results of the binding assays are shown in Figure 16. The constructs 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49) and 5-10xanti-CD3 (SEQ ID NO.:63) showed strong binding to CD3 on Jurkat cells and to CD19 on Kato cells.

Example 8.3. Purification of bispecific anti EpCAM constructs with deimmunized anti-CD3 part

The constructs comprising a deimmunized anti-CD3 region and an EpCAM-specific region were purified with a two-step purification process including immobilized metal affinity chromatography (IMAC) and gel filtration. Metal affinity chromatography (IMAC) and gel filtration were carried out as demonstrated in example 3.2.

A further high-resolution cation exchange chromatography was performed on a MiniS column (Amersham), equilibrated with 20mM MES buffer pH 5.5. The sample was diluted 1:3 with the same buffer before loading to the column. Bound protein was eluted with a 0-30% gradient gradient of 1 M NaCl in equilibration buffer. The eluted protein fractions were tested in the bioactivity assay. Table 14 shows the yields of the purified deimmunized EpCAM constructs. All the constructs could be efficiently

produced. Surprisingly, the construct 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63) had an extremely good yield of 2200 µg/l.

Table 14. Yields of the deimmunized EpCAM constructs

Construct	Yield of the monomer [µg purified protein per liter culture]
anti-CD3 (VH5/VL2)x4-7 (SEQ ID NO.:33)	112.5
3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49)	87.5
anti-CD3 (VH5/VL2)x3-1 (SEQ ID NO.:31)	442.5
5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63)	2200
anti-CD 3 (VH5/VL2)x5-10 (SEQ ID NO.:37)	80

Example 8.4 Cytotoxic assays of the bispecific anti-EpCAM constructs with deimmunized anti-CD3 part

In order to confirm the high bioactivity of the bispecific antibodies of the invention, a FACS based assay was carried out. CHO cells were transfected with epithelial cell adhesion molecule (EpCAM). A cell clone derived from this transfection, referred to as CHO-EpCAM cells, was used for the experiments.

For the cytotoxicity test, CHO-EpCAM ($1.5x10^7$) cells were washed free of serum two times with PBS and incubated with PKH26 dye (Sigma-Aldrich Co.) according to the manufacturers instructions. After staining, cells were washed two times with RPMI/10% FCS.

Cells were counted and mixed with CB15 effector cells. The CD4-positive T cell clone CB15 was kindly provided by Dr. Fickenscher, University of Erlangen/Nuernberg, Germany. Cells were cultured as recommended by the suppliers. The resulting cell suspension contained 400.000 target and 2 x 10^6 effector cells per ml. 50 µl of the mixture was used per well in a 96 well round bottom plate.

Antibodies were diluted in RPMI/10% FCS to the required concentration and 50 µl of this solution was added to the cell suspension. A standard reaction was incubated for 16 h at 37°C / 5% CO_2. Propidium iodide was added to a final concentration of 1 µg/ml. After 10 min of incubation at room temperature cells were analysed by FACS. PKH26 fluorescence was used for positive identification of target cells. Cytotoxicity was measured as ratio of PI positive over all target cells.

Sigmoidal dose response curves typically had R2 values >0.97 as determined by Prism Software (GraphPad Software Inc., San Diego, USA). The results of the cytotoxic assays are shown in Figures 17 and 18.

Example 8.5. Comparison of the productivity of bispecific molecules comprising an EpCAM binding part and a deimmunized CD3 binding part in CHO cells

In order to determine the productivity of a deimmunized construct protein L ELISA was perfomed. The productivity data was caluculated from batch cultures.

8.5.1 Cell Culture

CHO cell lines producing deimmunized (CHO-DHFR-) and non-deimmunized (CHO-DHFR- or CHO-K1) were cultivated in HyQ PF CHO LS medium + 4 mM L-Glutamine in a CO_2 incubator at 37°C and 5% CO_2. Cell numbers and viability were determined using Trypan Blue. Cell density was set to 1-2×10^5 cell/ml.

Cells were transferred to spinner flasks and thus adjusted to conditions of a stirred culture. Operational parameter settings were 80 rpm, 37°C and 5% CO_2 with gassing in a CO_2 incubator. Culture volume was in the 100–500 ml-range and cell density at inoculation in the range of 1-2×10^5 cells/ml. As for the subcultivation in T-flasks, cultures were centrifuged and resuspended in fresh pre-warmed medium at each passage. Cell density was set to 1-2×10^5 cells/ml.

For analysis of productivity data (Table 15) cells were cultivated up to 14 days (d) without any medium addition or exchange. Cell numbers and viability were determined daily using Trypan blue stain. Product concentrations in the supernatant were analyzed by Protein L ELISA.

8.5.2 Protein L ELISA

Quantitative binding of the bispecific molecules was carried out with rProtein L-coated microtiter plates. rProtein L is a recombinant form of the immunoglobulin-binding Protein L produced by Peptostreptococcus magnus. It has four binding domains and binds immunoglobulin through the light chain (κ). Bispecific molecules, which contain variable domains from two different light chains respectively parent antibodies, are also bound by rProtein L.

Microtiter plates were coated with rProtein L in PBS buffer (2 µg rProtein L/ml PBS buffer) overnight at 2-8°C. Following coating, remaining adsorption sites were blocked with of blocking buffer (2% BSA in PBS buffer). Then, the plates were frozen and stored at ≤18°C. Before use, the plates were thawed and washed with washing buffer (0.05% Tween 20 in PBS buffer) to remove the mixture of coating solution and blocking buffer.

Serial dilutions of cell-free cell culture supernatant in 1% BSA + 0.01% Tween 20 in PBS (dilution buffer) were analyzed. Bispecific anti-EpCAM(M79)xanti-CD3 was used as positive control in comparable dilutions.

Incubation was performed overnight at 2-8°C.

After washing rabbit anti-mouse IgG (1:5,000 in dilution buffer) was added and incubated for 60 min at room temperature. Goat anti-rabbit IgG labeled with alkaline phosphatase was added (1:1,000 in dilution buffer; 60 min at room temperature) after washing. pNPP substrate solution was added and the reaction was stopped by addition of 3 M NaOH. Absorbance was measured with an ELISA reader at 405 nm (reference filter 492 nm).

Table 15. Productivity of an deimmunized anti-EpCAM construct

Construct	**M79xanti-anti-CD3**		**5-10xanti-CD3 (VH5/VL2)**
Basic cell line	CHO-K1	CHO-dhfr-	CHO-dhfr-
Specific productivity	0.2-0.6 pg/cell per day	1-3 pg/cell per day	15-20 pg/cell per day
Maximal cell density	$3x10^6$ c/ml	$1.2-1.8x10^6$ c/ml	$1.5x10^6$ c/ml
Doubling time	17-20 h	25-30 h	25-30 h

Thus, the inventive 5-10xanti-CD3 (VH5/VL2) construct demonstrated much higher specific productivity (at least five times higher) than the prior art bispecific non-deimmunized EpCAM and CD3 binding antibody.

EPO - Munich
41
16. Okt. 2003

Claims

1. A cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain, wherein said first domain is deimmunized and comprises a CDR-H1 region, a CDR-H2 region and a CDR-H3 region, said CDR-H3 region comprising an amino acid sequence as depicted in SEQ ID NO. 96, 108,119, 120, 121, 122, 123, 124, 125, 126, or 127; and
wherein said first domain further comprises in its framework H1 the sequence VKK and wherein the transition sequence between framework H1 and CDRH1 region comprises the sequence Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF; SEQ ID NO: 233).

2. The cytotoxically active CD3 specific binding construct of claim 1 further comprising in said first domain a framework H3 comprising the sequence Met-Glu-Leu-Ser (MELS; SEQ ID NO: 234).

3. The cytotoxically active CD3 specific binding construct of claim 1 or 2 further comprising in said first domain a framework H3 comprising the sequence Ile-Thr-Thr-Asp-Lys (ITTDK; SEQ ID NO: 235).

4. The CD3 specific binding construct of any one of claims 1to 3, wherein said first domain which specifically binds to human CD3 comprises a framework H1 as shown in SEQ ID NO. 152 or 153.

5. The CD3 specific binding construct of any one of claims 1 to 4, wherein said first domain which specifically binds to human CD3 comprises a framework H2 as shown in SEQ ID NO. 156 or 157.

6. The CD3 specific binding construct of any one of claims 1 to 5, wherein said first domain which specifically binds to human CD3 comprises a framework H3 as shown in SEQ ID NO. 160 or 161.

7. The CD3 specific binding construct of any one of claims 1 to 6, wherein said first domain which specifically binds to human CD3 comprises a framework H4 as shown in SEQ ID NO. 164 or 165.

8. The CD3 specific binding construct of any one of claims 1 to 7, wherein said construct comprises
   (a) a CDR-H1 as depicted in SEQ ID NO 88; and
   (b) a CDR-H2 as depicted in SEQ ID NO 90 or 92.

9. The CD3 specific binding construct of any one of claims 1 to 8, wherein said construct comprises a V_H-region as depicted in SEQ ID NO.74 or 76.

10. The CD3 specific binding construct of any one of claims 1 to 9, wherein said construct comprises a CDR-L1 as depicted in SEQ ID NO. 98 or 100.

11. The CD3 specific binding construct of any one of claims 1 to 10, wherein said construct comprises a CDR-L2 as depicted in SEQ ID NO.102.

12. The CD3 specific binding construct of any one of claims 1 to 11, wherein said construct comprises a CDR-L3 as depicted in SEQ ID NO.104.

13. The CD3 specific binding construct of any one of claims 1 to 12 comprising a V_L region in its CD3-specific portion, wherein said V_L region is selected from the group consisting of SEQ ID NO 78, SEQ ID NO 80, SEQ ID NO 82 and SEQ ID NO 112.

14. The CD3 specific binding construct of any of claims 1 to 13, wherein said Ig-derived second domain is a scFv.

15. The CD3 specific binding construct of any of claims 1 to 14, wherein said Ig-derived second domain and/or (a) connecting linker-region(s) is/are humanized and/or deimmunized.

16. The CD3 specific binding construct of any of claims 1 to 15, wherein said Ig-

derived second domain comprises an antigen-interaction-site with specificity for a cell surface molecule.

17. The CD3 specific binding construct of claim 16, wherein said cell surface molecule is a tumor specific marker.

18. The CD3 specific binding construct of any of claims 16 or 17, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for a molecule selected from the group consisting of EpCAM, CCR5, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA,, MUC-1 (mucin), MUC2, MUC3, MUC4, $MUC5_{AC}$, $MUC5_{B}$, MUC7, βhCG, Lewis-Y, CD20, CD33, CD30, ganglioside GD3, 9-O-Acetyl-GD3, GM2, Globo H, fucosyl GM1, Poly SA, GD2, Carboanhydrase IX (MN/CA IX), CD44v6, Sonic Hedgehog (Shh), Wue-1, Plasma Cell Antigen, (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), CCR8, TNF-alpha precursor, STEAP, mesothelin, A33 Antigen, Prostate Stem Cell Antigen (PSCA), Ly-6; desmoglein 4, E-cadherin neo-epitope, Fetal Acetylcholine Receptor, CD25, CA19-9 marker, CA-125 marker and Muellerian Inhibitory Substance (MIS) Receptor type II, sTn (sialylated Tn antigen, TAG72), FAP (fibroblast activation antigen), endosialin, EGFRvIII, L6, SAS, CD63, TAG72, TF-antigen, Cora antigen, CD7, CD22, Igα, Igβ, G250, gp100, MT-MMPs, F19-antigen, CO-29 and EphA2.

19. The CD3 specific binding construct of any of claims 1 to 18, wherein said second Ig-derived binding domain comprises an antigen-interaction site with a specificity for EpCAM.

20. The CD3 specific binding construct of claim 19, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257,.259, 261, 263, 265, 267, 269, 271, 273, 275, 277,

279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

21. The CD3 specific binding construct of any of claims 1 to 18, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity CCR5.

22. The CD3 specific binding construct of claim 21,-wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO 206, 208, 210, 212, 214 or 216;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 205, 207, 209, 211, 213 or 215; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

23. The CD3 specific binding construct of any of claims 1 to 18, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for CD19.

24. The CD3 specific binding construct of claim 23, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO 190, 192, 194, 196, 198,200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 189, 191, 193, 195, 197, 199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406 or 408; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

25. The CD3 specific binding construct of any of claims 1 to 18, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for CD20.

26. The CD3 specific binding construct of claim 25, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO 218, 220, 222, 224, 226, or 228;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 217, 219, 221, 223, 225 or 227; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

27. A nucleic acid sequence encoding a CD3 specific binding construct according to any of claims 1 to 26.

28. A vector comprising a nucleic acid sequence according to claim 27.

29. The vector of claim 28, which further comprises a nucleic acid sequence which is a regulatory sequence operable linked to said nucleic acid sequence according to claim 27.

30. The vector of claim 28 or 29, wherein the vector is an expression vector.

31. A host transformed or transfected with a vector according to any of claims 28 to 30.

32. A process for the production of a CD3 specific binding construct according to any of claims 1 to 26 said process comprising culturing a host of claim 31 under conditions allowing the expression of the polypeptide construct and recovering the produced polypeptide construct from the culture.

33. A composition comprising a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31 and, optionally, a proteinaceous compound capable of providing an activation signal for immune effector cells.

34. The composition of claim 33, which is a pharmaceutical composition further comprising, optionally, suitable formulations of carrier, stabilizers and/or excipients.

35. The composition of claim 33, which is a diagnostic composition further comprising, optionally, means and methods for detection.

36. Use of a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31 for the preparation of a pharmaceutical composition for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases.

37. A method for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases comprising the adminsitraion of a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31 to a subject in need of such a prevention, treatment or amelioration .

38. The method of claim 37, wherein said subject is a human.

39. The method of any one of claims 37 or 38 further comprising, the administration of a proteinaceous compound capable of providing an activation signal for immune effector cells.

40. The method of claim 39, wherein said proteinaceous compound is administered simultaneously or non-simultaneously with a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31.

41. A kit comprising a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31.

Abstract

The present invention provides a cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain. Furthermore, a nucleic acid sequence encoding a CD3 specific binding construct of the invention is provided. Further aspects of the invention are vectors and host cells comprising said nucleic acid sequence, a process for the production of the construct of the invention and composition comprising said construct. The invention also provides the use of said constructs for the preparation of pharmacutical compositions for the treatment of particular diseases, a method for the treatment of particular diseases and a kit comprising the binding construct of the invention.

Figure 1

Anti-CD3 WT

GATATCAAACTGCAGCAGTCAGGGGCTGAACTGGCAAGACCTGGGGCCTCAGTGAAGATGTCCT
GCAAGACTTCTGGCTACACCTTTACTAGGTACACGATGCACTGGGTAAAACAGAGGCCTGGACA
GGGTCTGGAATGGATTGGATACATTAATCCTAGCCGTGGTTATACTAATTACAATCAGAAGTTC
AAGGACAAGGCCACATTGACTACAGACAAATCCTCCAGCACAGCCTACATGCAACTGAGCAGCC
TGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGATATTATGATGATCATTACTGCCTTGA
CTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCAGTCGAAGGTGGAAGTGGAGGTTCTGGT
GGAAGTGGAGGTTCAGGTGGAGTCGACGACATTCAGCTGACCCAGTCTCCAGCAATCATGTCTG
CATCTCCAGGGGAGAAGGTCACCATGACCTGCAGAGCCAGTTCAAGTGTAAGTTACATGAACTG
GTACCAGCAGAAGTCAGGCACCTCCCCCAAAAGATGGATTTATGACACATCCAAAGTGGCTTCT
GGAGTCCCTTATCGCTTCAGTGGCAGTGGGTCTGGGACCTCATACTCTCTCACAATCAGCAGCA
TGGAGGCTGAAGATGCTGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCACGTTCGG
TGCTGGGACCAAGCTGGAGCTGAAA

AA Sequence

DIKLQQSGAELARPGASVKMSCKTSGYTFTRYTMHWVKQRPGQGLEWIGYINPSRGYTNYNQKF
KDKATLTTDKSSSTAYMQLSSLTSEDSAVYYCARYYDDHYCLDYWGQGTTLTVSSVEGGSGGSG
GSGGSGGVDDIQLTQSPAIMSASPGEKVTMTCRASSSVSYMNWYQQKSGTSPKRWIYDTSKVAS
GVPYRFSGSGSGTSYSLTISSMEAEDAATYYCQQWSSNPLTFGAGTKLELK

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Fig. 2 A

VH2

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYAQKLQGRVTMTTDTSTSTAYMELSSLRSEDTATYYCARYYDDHYCLDYWG
QGTTVTVSS

VH3

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYAQKLQGRVTMTTDTSTSTAYLQMNSLKTEDTAVYYCARYYDDHYCLDYWG
QGTTVTVSS

VH5

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDTATYYCARYYDDHYCLDYWG
QGTTVTVSS

VH7

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYNQKFKDRVTITTDKSTSTAYMELSSLRSEDTAVYYCARYYDDHYCLDYWG
QGTTVTVSS

Fig. 2 A (cont.)

VL1

DIQMTQSPSSLSASVGDRVTITCRASQSVSYMNWYQQKPGKAPKRWIYDT
SKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQQWSSNPLTFGGG
TKVEIK

VL2

DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDT
SKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQQWSSNPLTFGGG
TKVEIK

VL3

DIVLTQSPATLSLSPGERATLTCRASSSVSYMNWYQQKPGKAPKRWIYDT
SKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQQWSSNPLTFGGG
TKVEIK

Fig. 2 B

VH2

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACCTGGGGCCTCAGTGAAGGTGTCCTGC
AAGGCTTCTGGCTACACCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCTGGACAGGGT
CTGGAATGGATTGGATACATTAATCCTAGCCGTGGTTATACTAATTACGCACAGAAGTTGCAGGGC
CGCGTCACAATGACTACAGACACTTCCACCAGCACAGCCTACATGGAACTGAGCAGCCTGCGTTCT
GAGGACACTGCAACCTATTACTGTGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGGGC
CAAGGCACCACGGTCACCGTCTCCTCA

VH3

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACCTGGGGCCTCAGTGAAGGTGTCCTGC
AAGGCTTCTGGCTACACCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCTGGACAGGGT
CTGGAATGGATTGGATACATTAATCCTAGCCGTGGTTATACTAATTACGCACAGAAGTTGCAGGGC
CGCGTCACAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAAATGAACAGCCTGAAAACT
GAGGACACTGCAGTCTATTACTGTGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGGGC
CAAGGCACCACGGTCACCGTCTCCTCA

VH5

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACCTGGGGCCTCAGTGAAGGTGTCCTGC
AAGGCTTCTGGCTACACCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCTGGACAGGGT
CTGGAATGGATTGGATACATTAATCCTAGCCGTGGTTATACTAATTACGCAGACAGCGTCAAGGGC
CGCTTCACAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAACTGAGCAGCCTGCGTTCT
GAGGACACTGCAACCTATTACTGTGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGGGC
CAAGGCACCACGGTCACCGTCTCCTCA

Fig. 2 B (cont.)

VH7

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACCTGGGGCCTCAGTGAAGGTGTCCTGC
AAGGCTTCTGGCTACACCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCTGGACAGGGT
CTGGAATGGATTGGATACATTAATCCTAGCCGTGGTTATACTAATTACAATCAGAAGTTCAAGGAC
CGCGTCACAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAACTGAGCAGCCTGCGTTCT
GAGGACACTGCAGTCTATTACTGTGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGGGC
CAAGGCACCACGGTCACCGTCTCCTCA

Fig. 2 B (cont.)

VL1

GACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCATCTGTCGGGGACCGTGTCACCATCACC
TGCAGAGCCAGTCAAAGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAAGGCACCCAAA
AGATGGATTTATGACACATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCT
GGGACCGACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA
CAGTGGAGTAGTAACCCGCTCACGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

VL2

GACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGTCTCCAGGGGAGCGTGCCACCCTGAGC
TGCAGAGCCAGTCAAAGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAAGGCACCCAAA
AGATGGATTTATGACACATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCT
GGGACCGACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA
CAGTGGAGTAGTAACCCGCTCACGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

VL3

GACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGTCTCCAGGGGAGCGTGCCACCCTGACC
TGCAGAGCCAGTTCAAGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAAGGCACCCAAA
AGATGGATTTATGACACATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCT
GGGACCGACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA
CAGTGGAGTAGTAACCCGCTCACGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

Fig. 2 C

vH CDR1	
Wt anti-CD3	GYTFTRYTMH
VH2,3	GYTATRYTMH
VH5,7	GYTFTRYTMH
vH CDR2	
WT anti-CD3,	
VH7	YINPSRGYTNYNQKFKD
VH5	YINPSRGYTNYADSVKG
VH2, 3	YINPSRGYTNYAQKLQG
vH CDR3	
WT anti-CD3,	
VH2, 3, 5, 7	YYDDHYCLDY
vK CDR1	
WT anti-CD3,	
VL3	RASSSVSYMN
VL1, 2	RASQSVSYMN
vK CDR2	
WT anti-CD3,	
VL1, 2, 3	DTSKVAS
vK CDR3	
WT anti-CD3,	
VL1, 2, 3	QQWSSNPLT

Fig. 2 D

vH CDR1	
WT anti-CD3	GGCTACACCTTTACTAGGTACACGATG CAC
VH2,3	GGCTACACCGCTACTAGGTACACGATG CAC
VH5,7	GGCTACACCTTTACTAGGTACACGATG CAC
vH CDR2	
WT anti-CD3, VH7	TACATTAATCCTAGCCGTGGTTATACT AATTACAATCAGAAGTTCAAGGAC
VH5	TACATTAATCCTAGCCGTGGTTATACT AATTACGCAGACAGCGTCAAGGGC
VH2,3	TACATTAATCCTAGCCGTGGTTATACT AATTACGCACAGAAGTTGCAGGGC
VH CDR3	
WT anti-CD3, VH2, 3, VH5, 7	TATTATGATGATCATTACTGCCTT GACTAC

Fig. 2 D (cont.)

vK CDR1

WT anti-CD3, VL3	AGAGCCAGTTCAAGTGTAAGTTACATG AAC
VL1, 2	AGAGCCAGTCAAAGTGTAAGTTACATG AAC

vK CDR2

WT anti-CD3, VL1-3	ACACATCCAAAGTGGCTTCT

VK CDR3

WT anti-CD3, VL1-3	CAACAGTGGAGTAGTAACCCGCTCACG

Figure 3

A) anti-CD3 (VH2/VL1)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) anti-CD3 (VH2/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYME
LSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIQMTQSPSSLSASVGDRVTITCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 3

C) anti-CD3 (VH2/VL2)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH2/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYME
LSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 3

E) anti-CD3 (VH2/VL3)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGACCTGCAGAGCCAGTTCA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

F) anti-CD3 (VH2/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYME
LSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLTCRASS
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 4

A) anti-CD3 (VH3/VL1)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAA
ATGAACAGCCTGAAAACTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) anti-CD3 (VH3/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQ
GLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYLQMNSL
KTEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGTSTGSGG
SGGSGGADDIQMTQSPSSLSASVGDRVTITCRASQSVSYMNWY
QQKPGKAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLE
AEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 4

C) anti-CD3 (VH3/VL2)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAA
ATGAACAGCCTGAAAACTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH3/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYLQ
MNSLKTEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 4

E) anti-CD3 (VH3/VL3)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAA
ATGAACAGCCTGAAAACTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGACCTGCAGAGCCAGTTCA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

F) anti-CD3 (VH3/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYLQ
MNSLKTEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLTCRASS
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 5

A) CD3 (VH5/VL1)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCAGACAGCGTCAAGGGCCGCTTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) CD3 (VH5/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYME
LSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIQMTQSPSSLSASVGDRVTITCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 5

C) anti-CD3 (VH5/VL2)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCAGACAGCGTCAAGGGCCGCTTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH5/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYME
LSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 5

E) anti-CD3 (VH5/VL3)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCAGACAGCGTCAAGGGCCGCTTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGACCTGCAGAGCCAGTTCA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

F) anti-CD3 (VH5/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYME
LSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLTCRASS
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 6

A) anti-CD3 (VH7/VL1)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACAATCAGAAGTTCAAGGACCGCGTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) anti-CD3 (VH7/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYNQKFKDRVTITTDKSTSTAYME
LSSLRSEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIQMTQSPSSLSASVGDRVTITCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 6

C) anti-CD3 (VH7/VL2)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACAATCAGAAGTTCAAGGACCGCGTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH7/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYNQKFKDRVTITTDKSTSTAYME
LSSLRSEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 6

E) anti-CD3(VH7/VL3)

GACGTCCAACTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACAATCAGAAGTTCAAGGACCGCGTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAGTGGAGGTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGACCTGCAGAGCCAGTTCA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

F) anti-CD3(VH7/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYNQKFKDRVTITTDKSTSTAYME
LSSLRSEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLTCRASS
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 7A

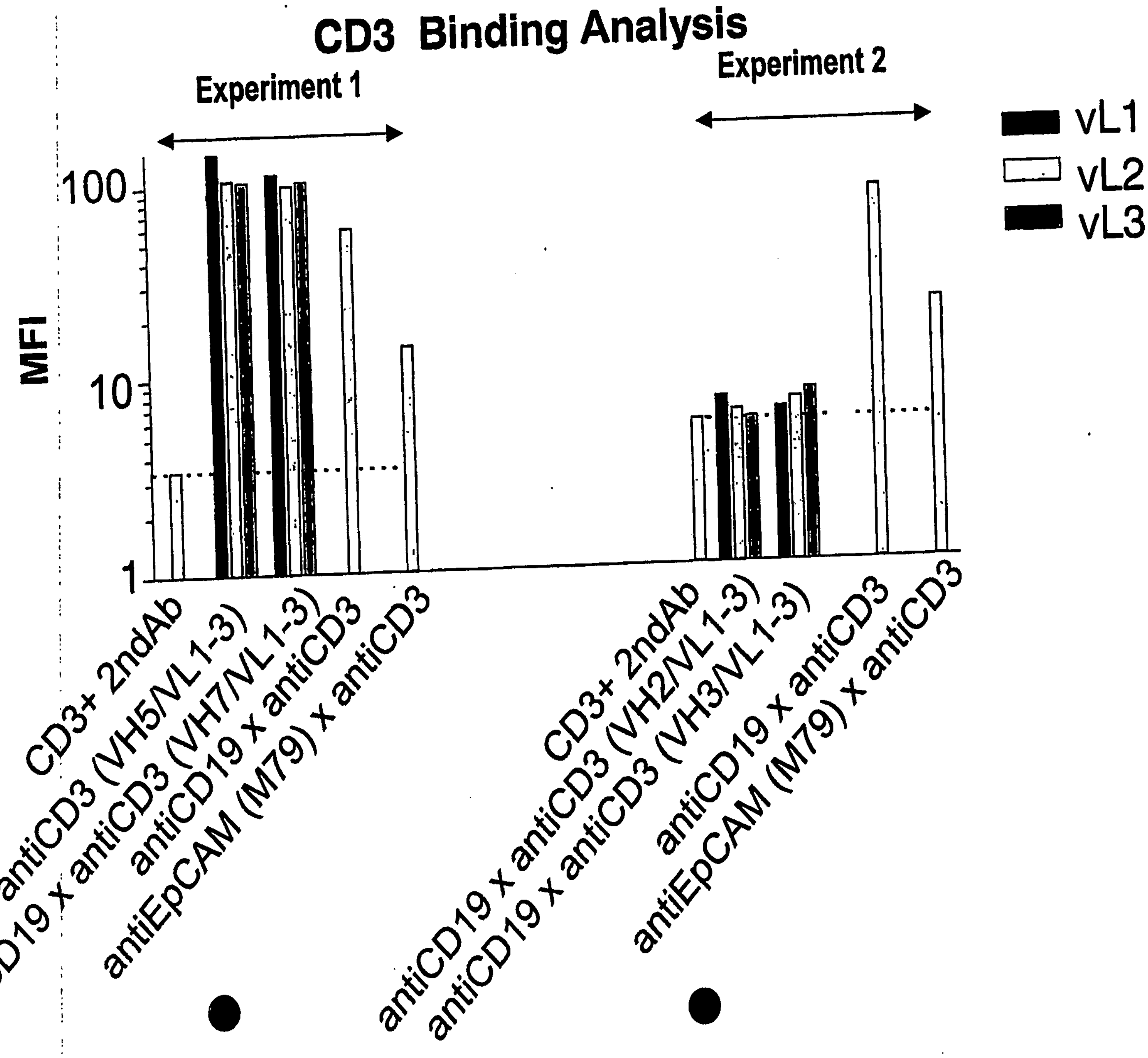

CD3 Binding Analysis
Experiment 1
Experiment 2
vL1
vL2
vL3
MFI
100
10
1
CD3+ 2ndAb
antiCD19 x antiCD3 (VH5/VL1-3)
antiCD19 x antiCD3 (VH7/VL1-3)
antiCD19 x antiCD3
antiEpCAM (M79) x antiCD3
CD3+ 2ndAb
antiCD19 x antiCD3 (VH2/VL1-3)
antiCD19 x antiCD3 (VH3/VL1-3)
antiCD19 x antiCD3
antiEpCAM (M79) x antiCD3

Figure 7B

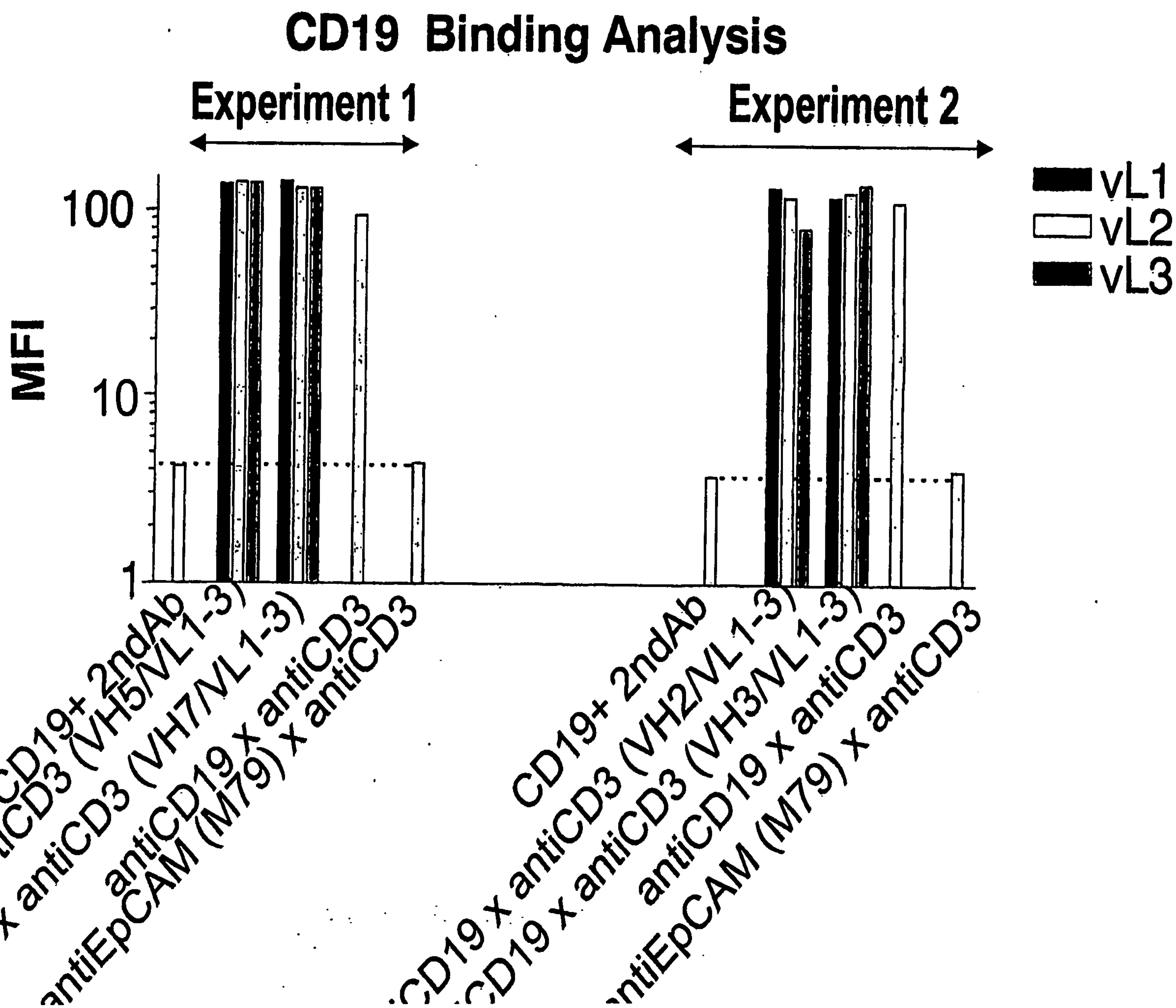

CD19 Binding Analysis
Experiment 1
Experiment 2
vL1
vL2
vL3
MFI
100
10
1
CD19+ 2ndAb
CD19 x antiCD3 (VH5/VL1-3)
CD19 x antiCD3 (VH7/VL1-3)
antiCD19 x antiCD3
antiEpCAM (M79) x antiCD3
CD19+ 2ndAb
CD19 x antiCD3 (VH2/VL1-3)
CD19 x antiCD3 (VH3/VL1-3)
antiCD19 x antiCD3
antiEpCAM (M79) x antiCD3

Figure 8

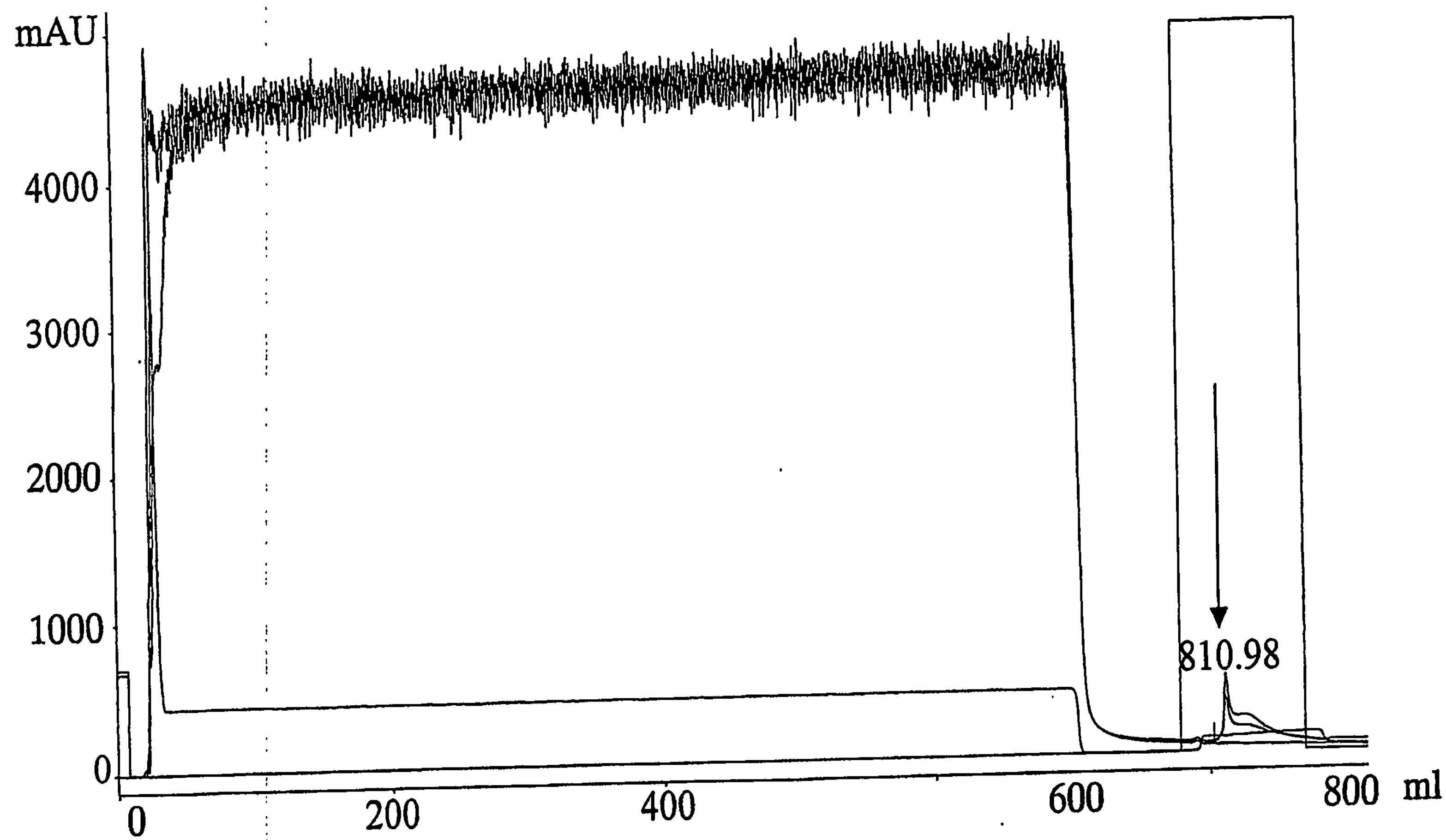


Figure 9

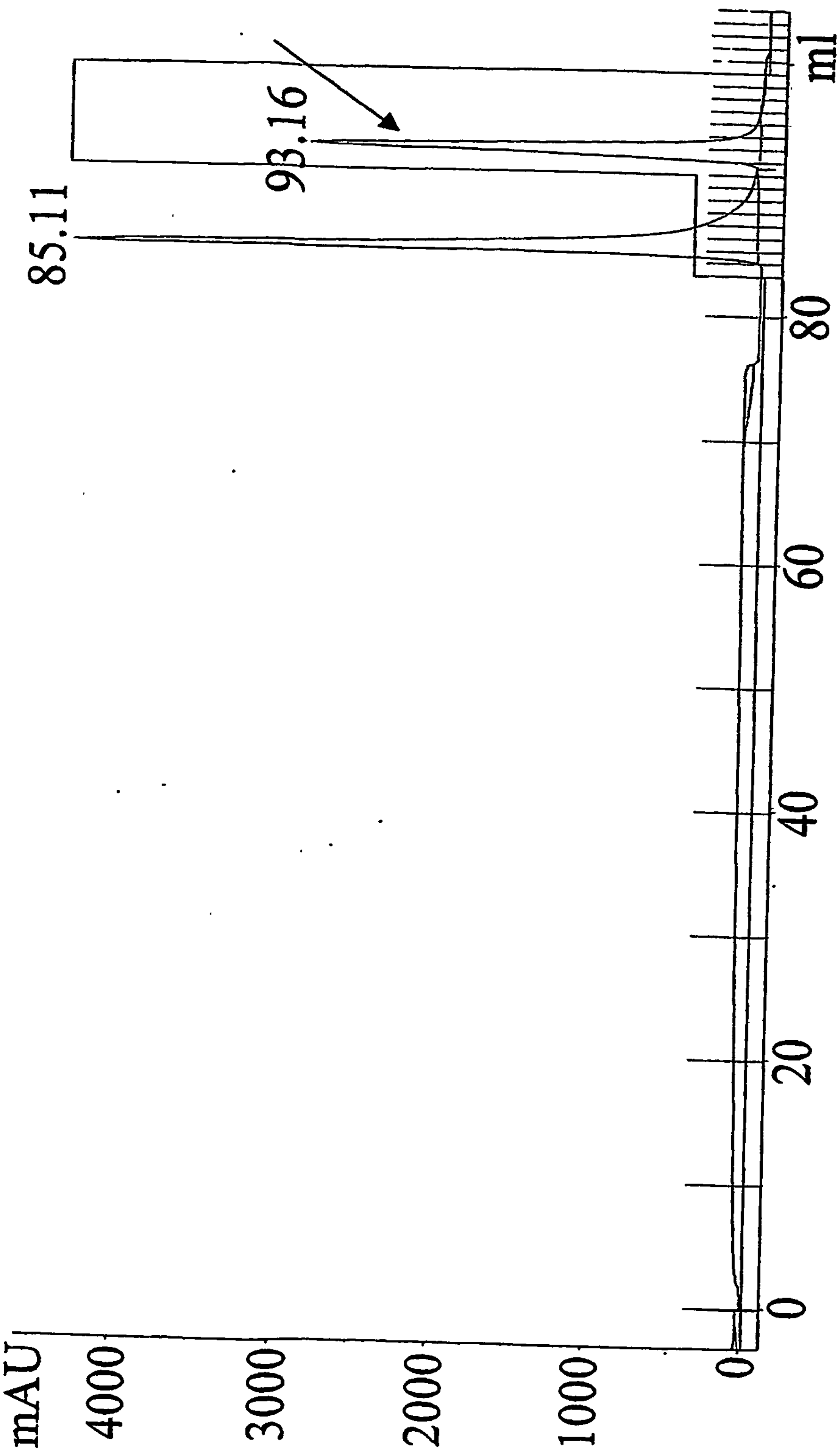


Figure 10

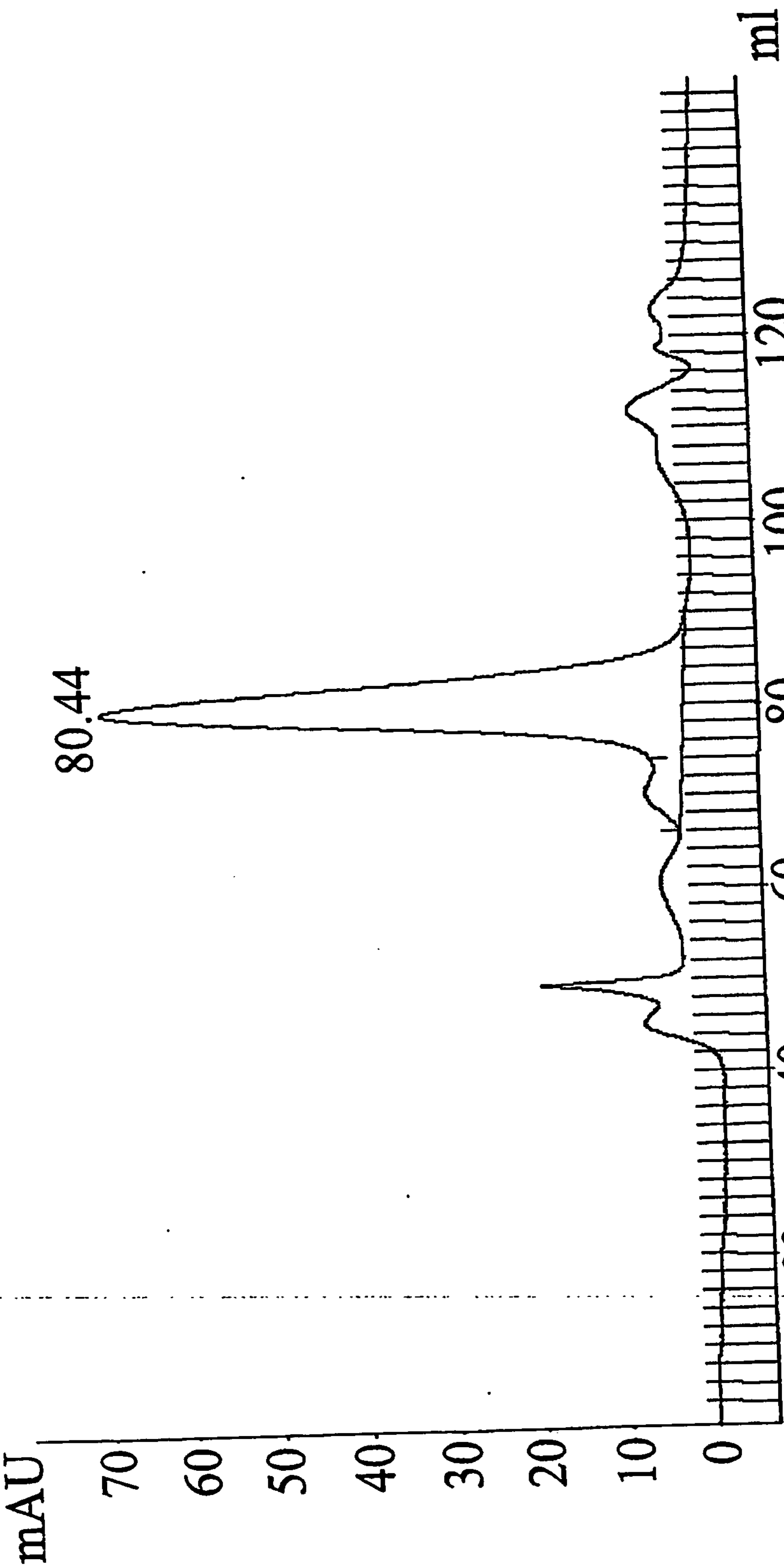
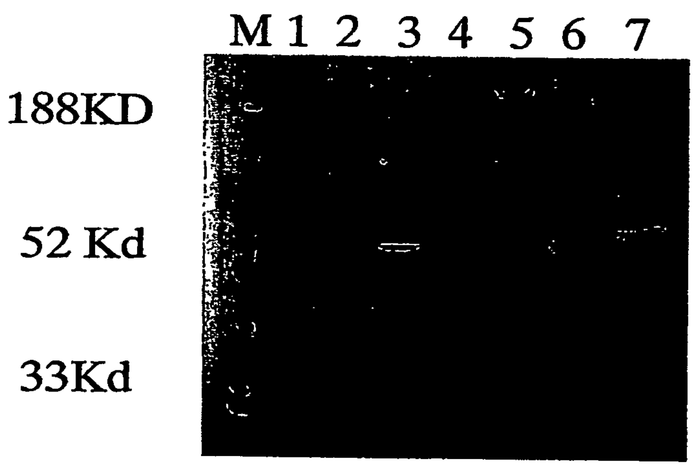


Figure 11

A)



B)

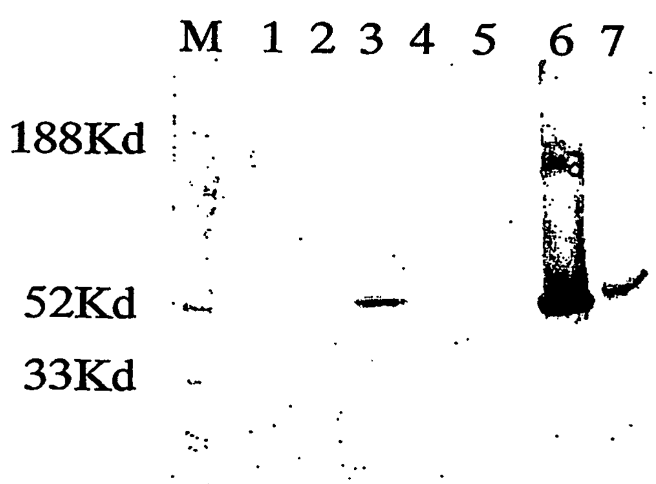


Figure 12A

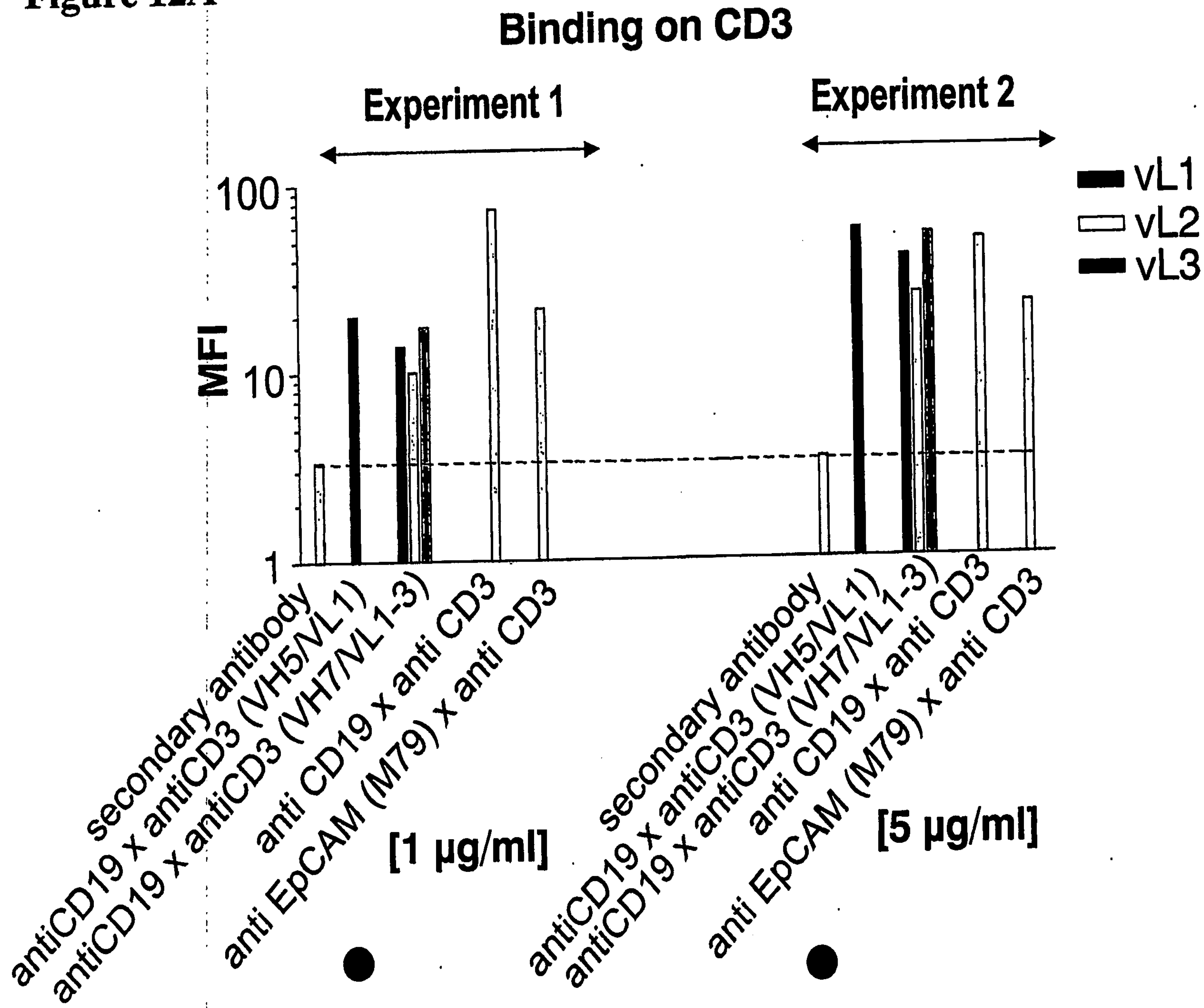

Binding on CD3
Experiment 1
Experiment 2
vL1
vL2
vL3
MFI
100
10
1
secondary antibody
antiCD19 x antiCD3 (VH5/VL1)
antiCD19 x antiCD3 (VH7/VL1-3)
anti CD19 x anti CD3
anti EpCAM (M79) x anti CD3
[1 µg/ml]
secondary antibody
antiCD19 x antiCD3 (VH5/VL1)
antiCD19 x antiCD3 (VH7/VL1-3)
anti CD19 x anti CD3
anti EpCAM (M79) x anti CD3
[5 µg/ml]

Figure 12B

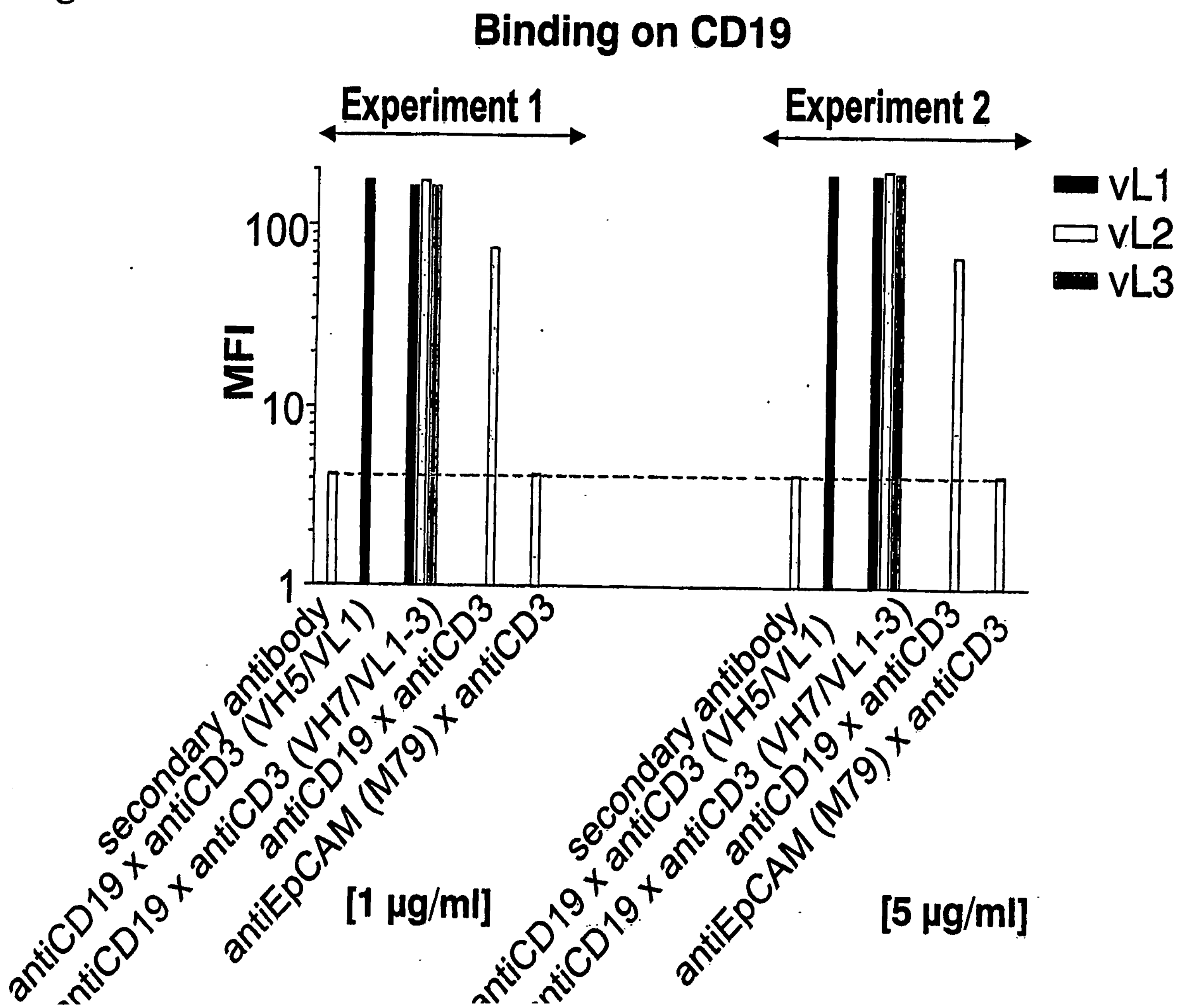

Binding on CD19
Experiment 1
Experiment 2
vL1
vL2
vL3
MFI
100
10
1
secondary antibody
antiCD19 x antiCD3 (VH5/VL1)
antiCD19 x antiCD3 (VH7/VL1-3)
antiCD19 x antiCD3
antiEpCAM (M79) x antiCD3
[1 µg/ml]
[5 µg/ml]

Figure 13

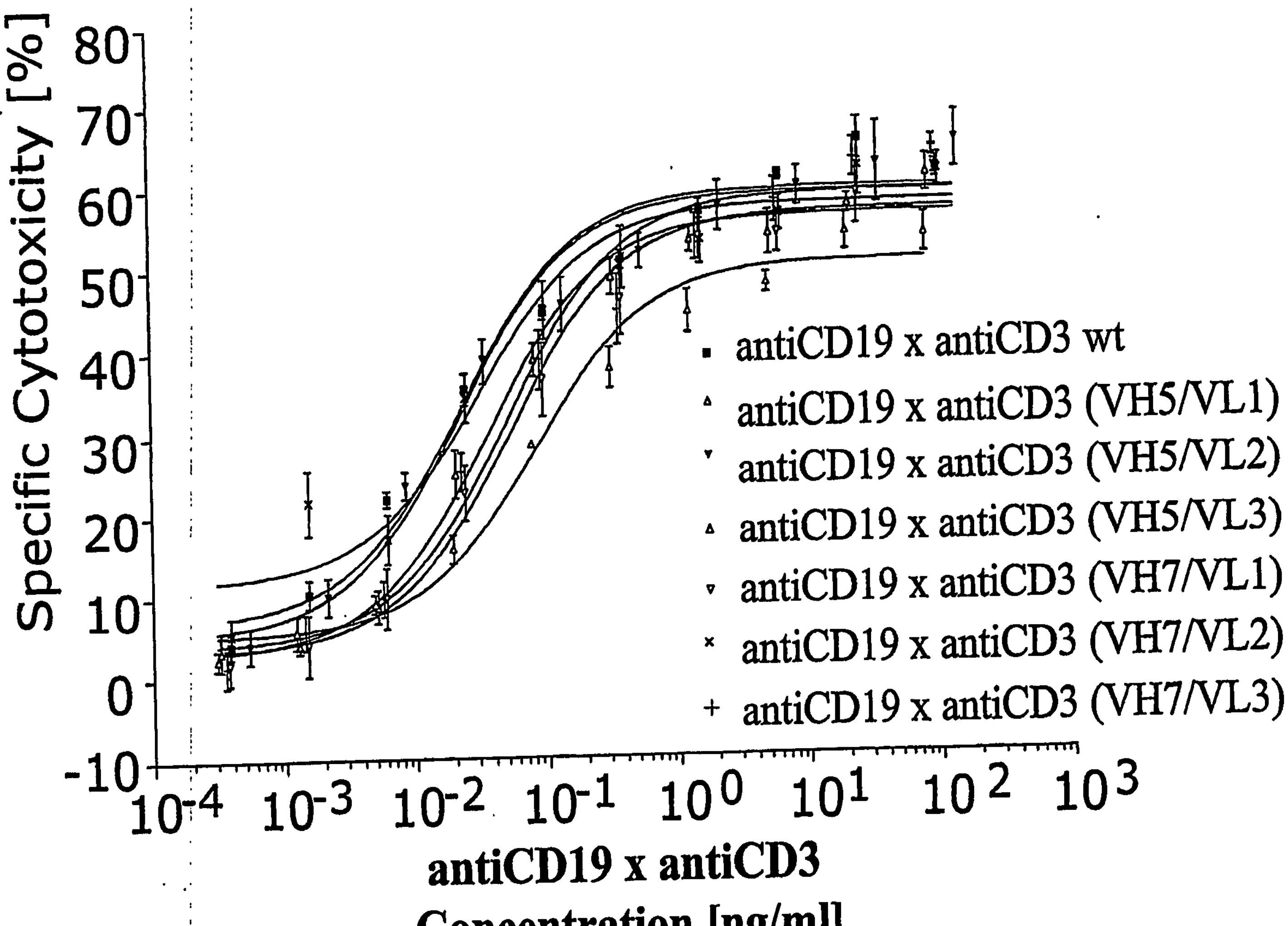

Specific Cytotoxicity [%]
80
70
60
50
40
30
20
10
0
-10
10-4
10-3
10-2
10-1
100
101
102
103
antiCD19 x antiCD3 wt
antiCD19 x antiCD3 (VH5/VL1)
antiCD19 x antiCD3 (VH5/VL2)
antiCD19 x antiCD3 (VH5/VL3)
antiCD19 x antiCD3 (VH7/VL1)
antiCD19 x antiCD3 (VH7/VL2)
antiCD19 x antiCD3 (VH7/VL3)
antiCD19 x antiCD3
Concentration [ng/ml]

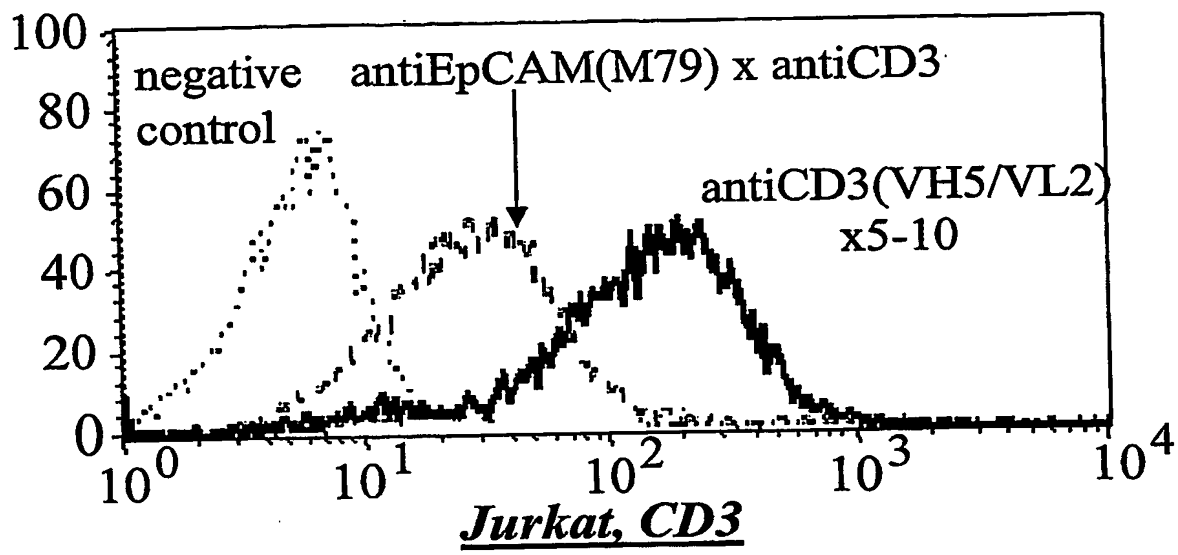
Figure 14

	FR1 CDR1 FR2 CDR2
nondeimmunized anti-CD3	DIKLQQSGAELARPGASVKMSCKTSGYTFTRYTMHWVKQRPGQGLEWIGYINPSRGYTNYNQKFKD
anti-CD3 VH5	DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSVKG
anti-CD3 VH7	DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYNQKFKD
anti-CD3 VH2	DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAQKLQG
anti-CD3 VH3	DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAQKLQG

	FR3 CDR3 FR4
nondeimmunized anti-CD3	KATLTTDKSSSTAYMQLSSLTSEDSAVYYCARYYDDHYCLDYWGQGTTLTVSS
anti-CD3 VH5	RFTITTDKSTSTAYMELSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSS
anti-CD3 VH7	RVTITTDKSTSTAYMELSSLRSEDTAVYYCARYYDDHYCLDYWGQGTTVTVSS
anti-CD3 VH2	RVTMTTDTSTSTAYMELSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSS
anti-CD3 VH3	RVTMTTDTSTSTAYLQMNSLKTEDTAVYYCARYYDDHYCLDYWGQGTTVTVSS

Figure 15 A

antiCD3(VH5/VL2) x 5-10 (SEQ ID NO: 37)



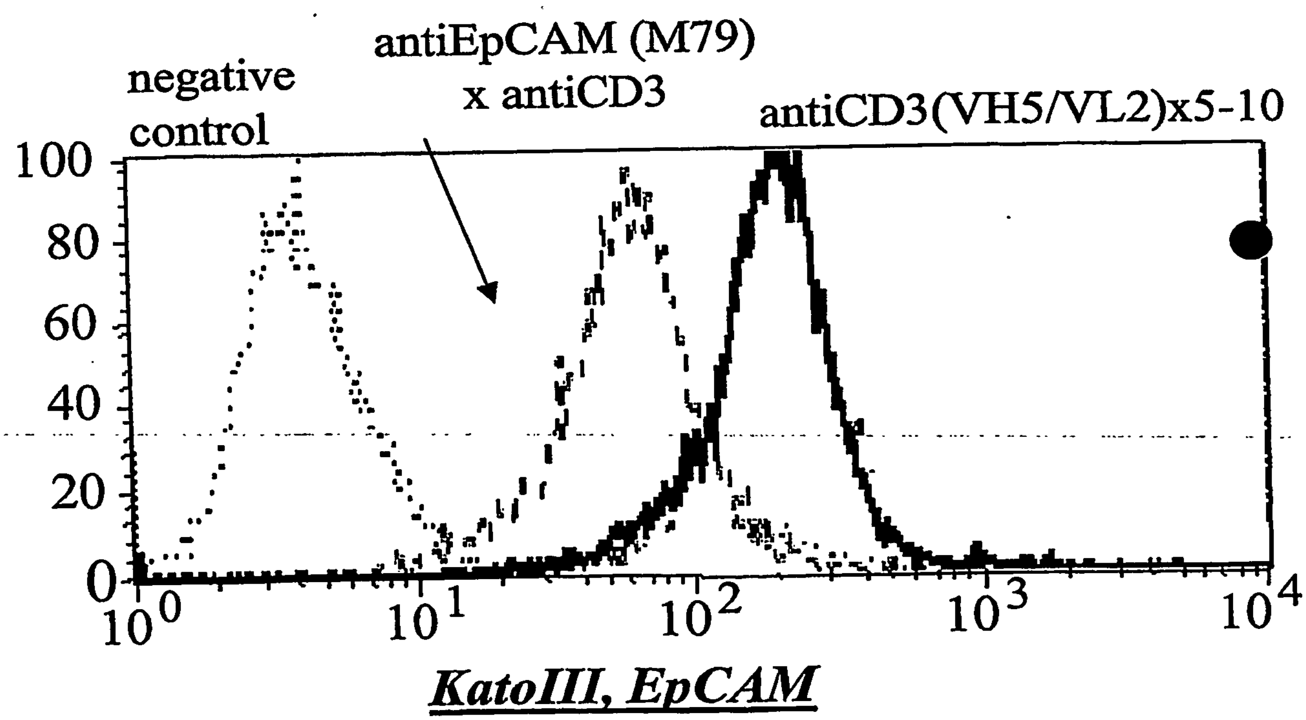
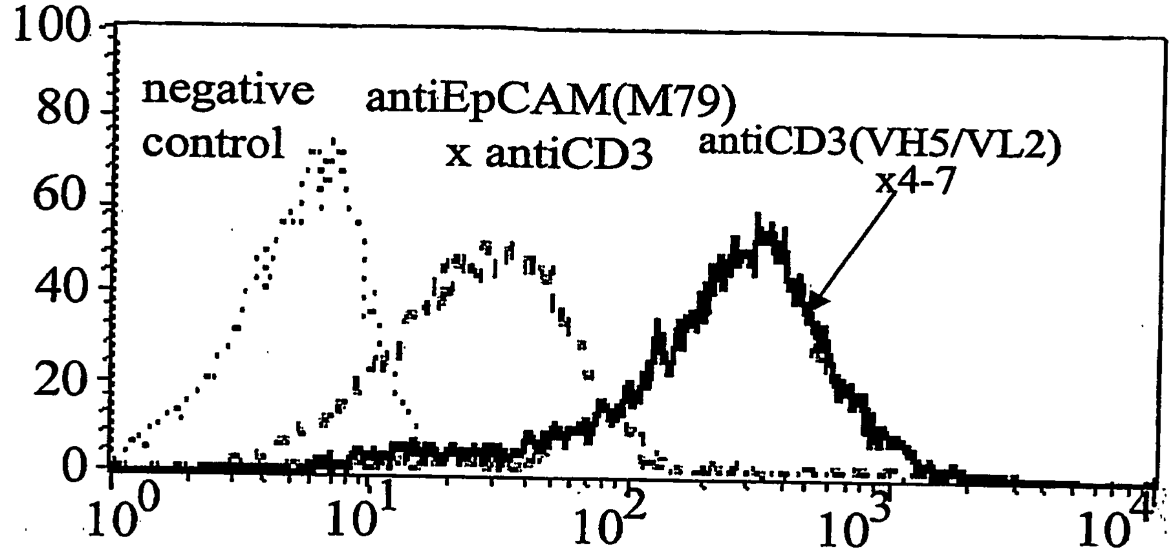
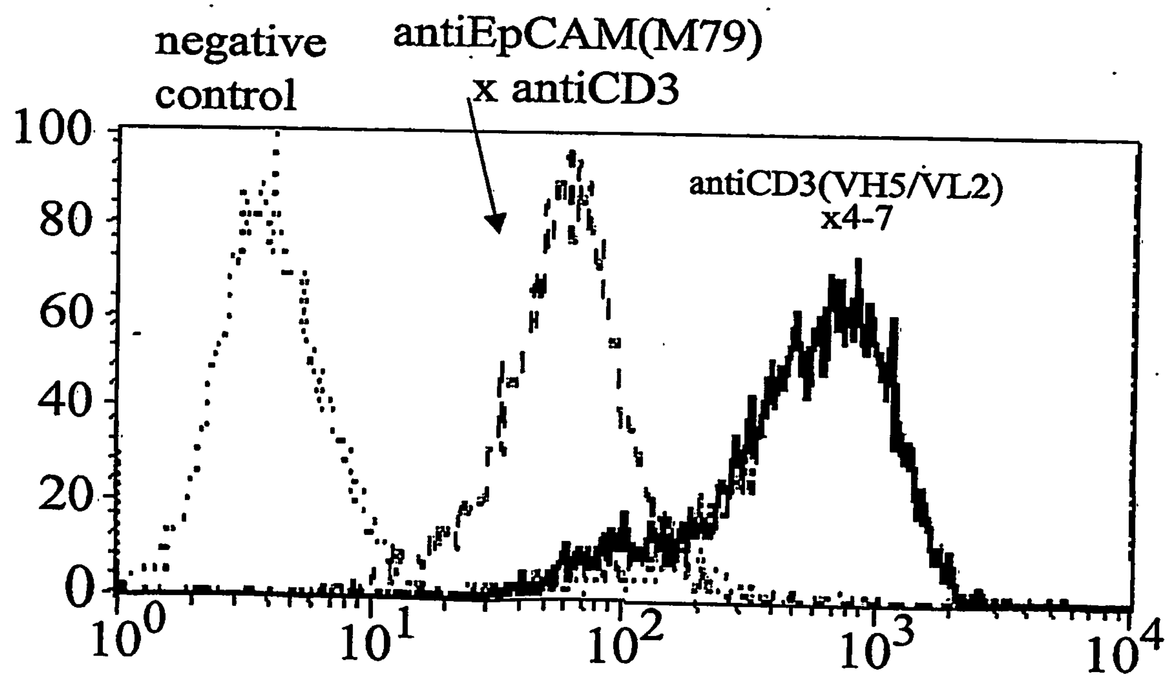


Figure 15B

antiCD3(VH5/VL2) x 4-7 (SEQ ID NO:33)



Jurkat, CD3



KatoIII, EpCAM

Figure 15C

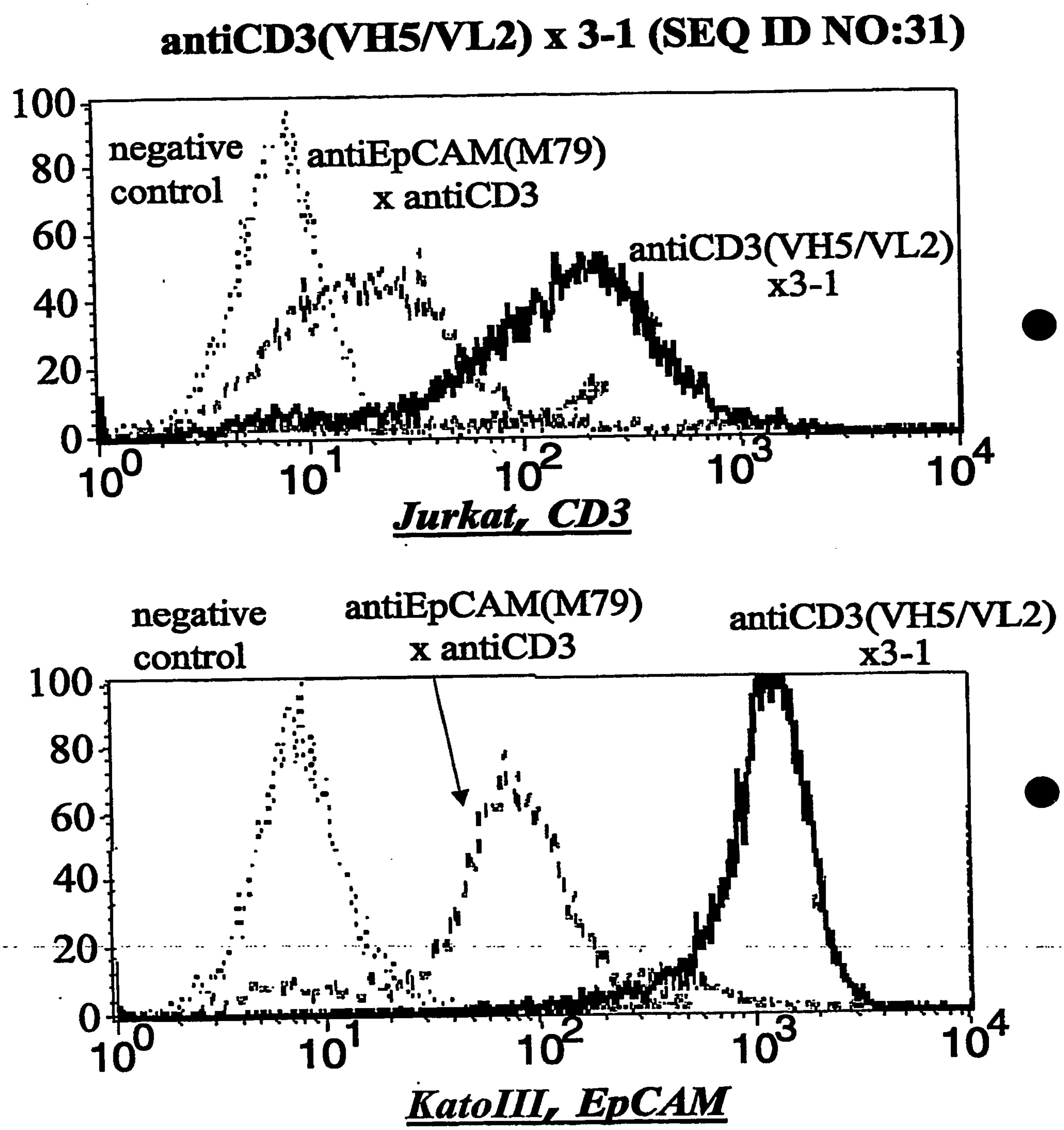

antiCD3(VH5/VL2) x 3-1 (SEQ ID NO:31)
100
80
60
40
20
0
negative control
antiEpCAM(M79) x antiCD3
antiCD3(VH5/VL2) x3-1
10^0
10^1
10^2
10^3
10^4
Jurkat, CD3
negative control
antiEpCAM(M79) x antiCD3
antiCD3(VH5/VL2) x3-1
100
80
60
40
20
0
10^0
10^1
10^2
10^3
10^4
KatoIII, EpCAM

Figure 15 D

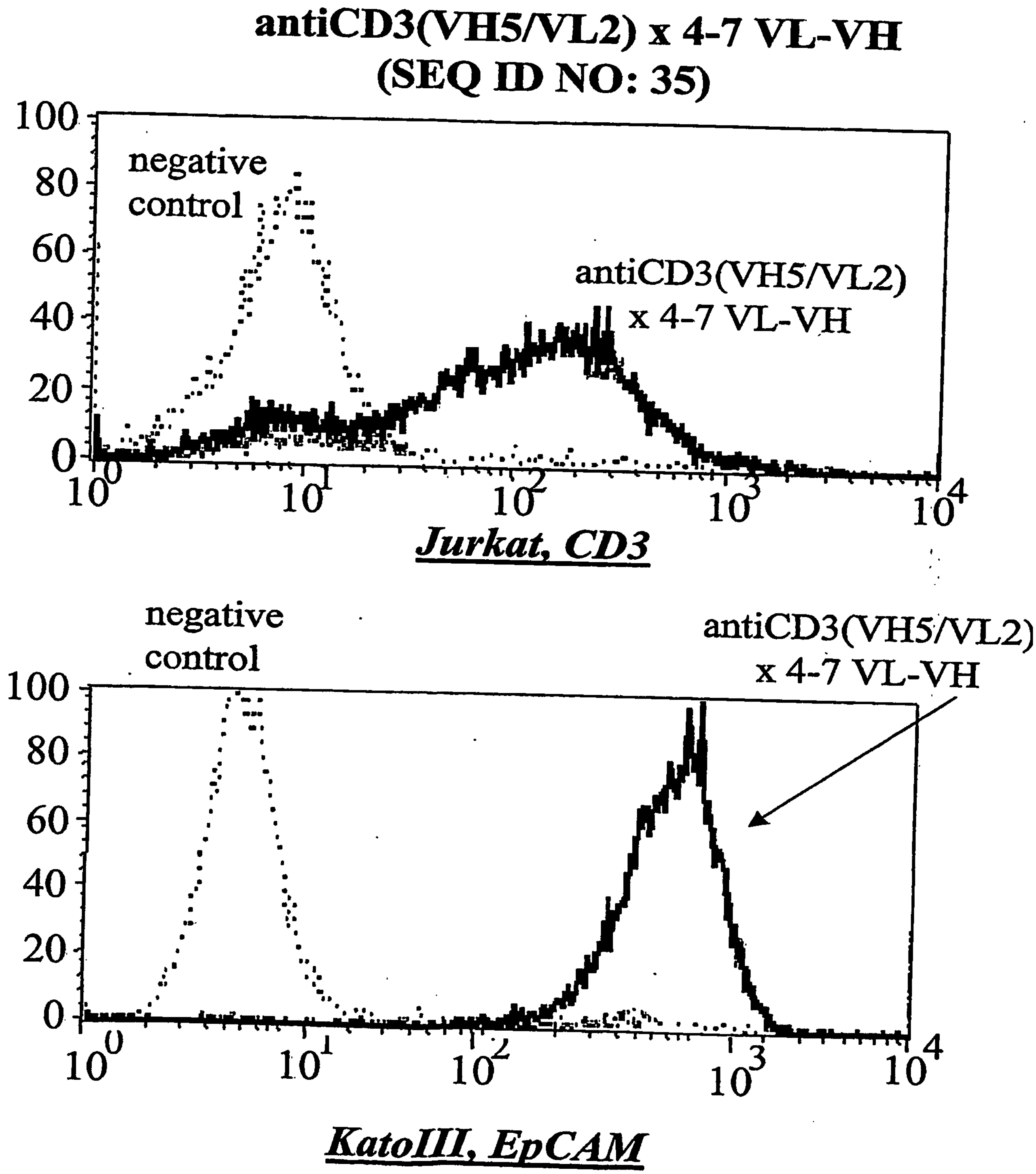
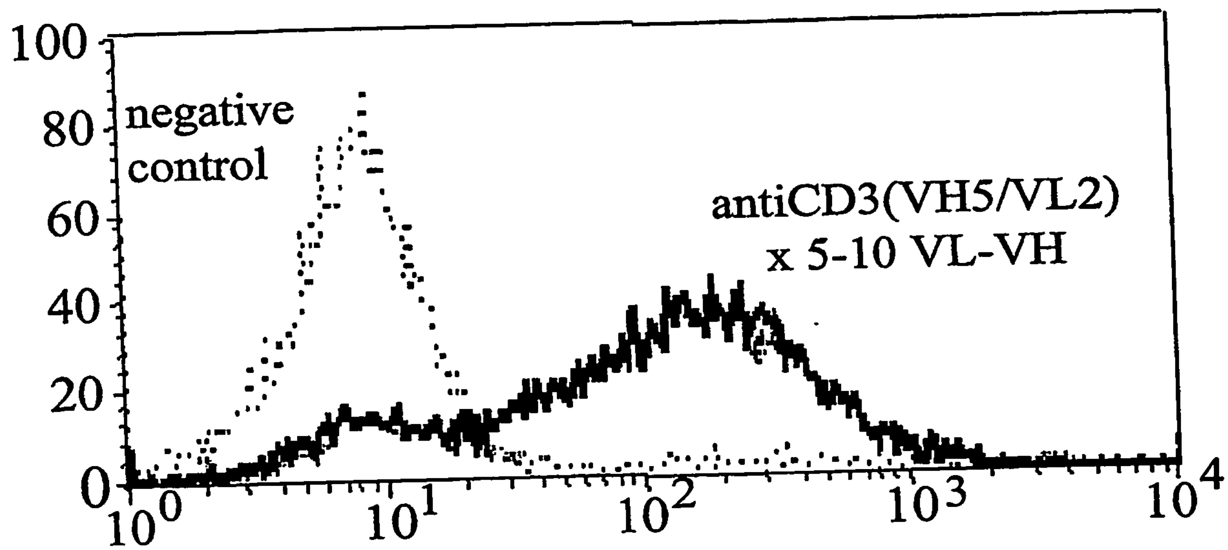
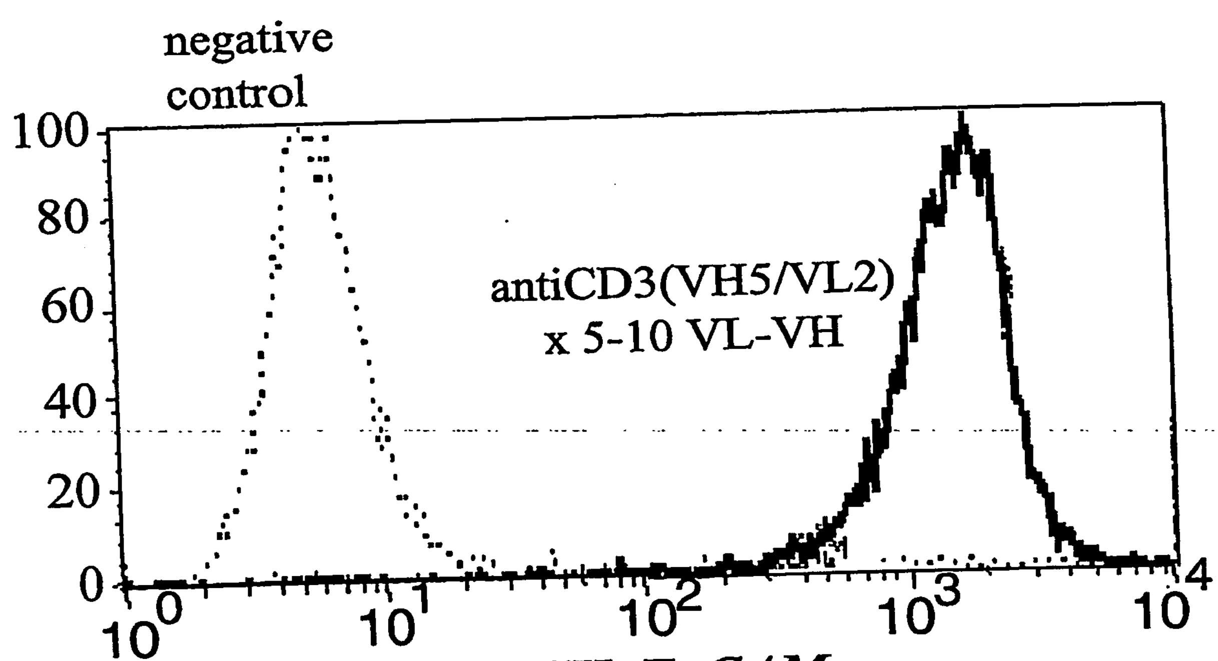

antiCD3(VH5/VL2) x 4-7 VL-VH
(SEQ ID NO: 35)
negative control
antiCD3(VH5/VL2) x 4-7 VL-VH
Jurkat, CD3
negative control
antiCD3(VH5/VL2) x 4-7 VL-VH
KatoIII, EpCAM

Figure 15 E

antiCD3(VH5/VL2) x 5-10 VL-VH (SEQ ID NO:39)



Jurkat, CD3

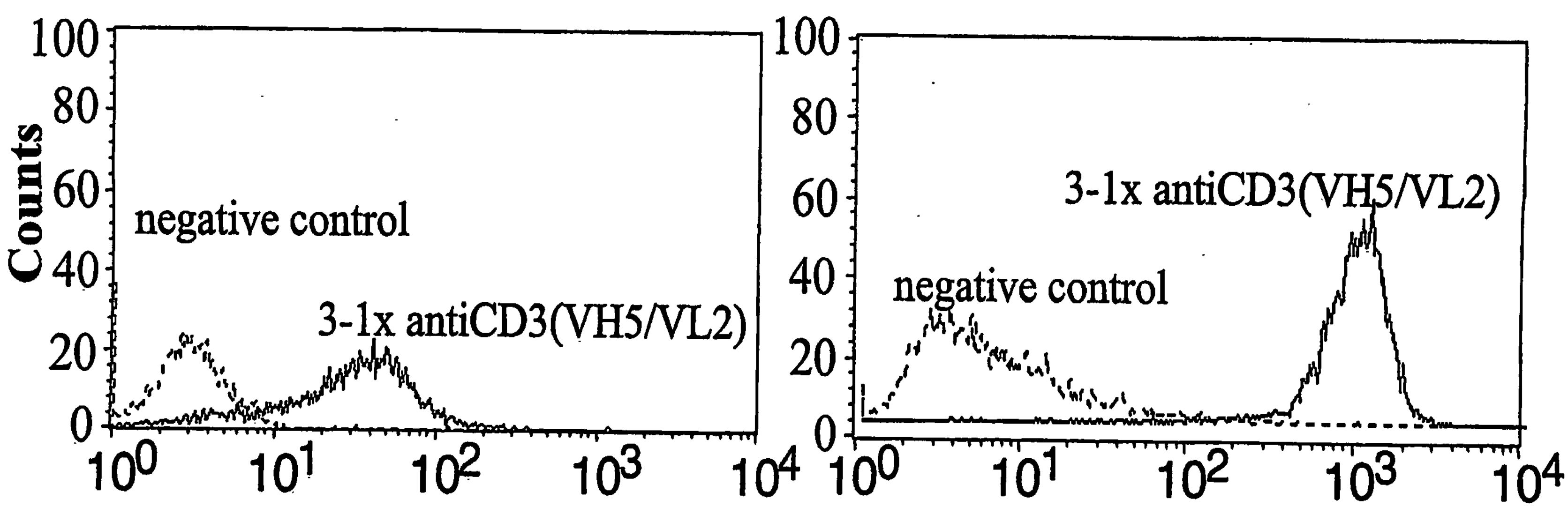


KatoIII, EpCAM

Figure 16 A

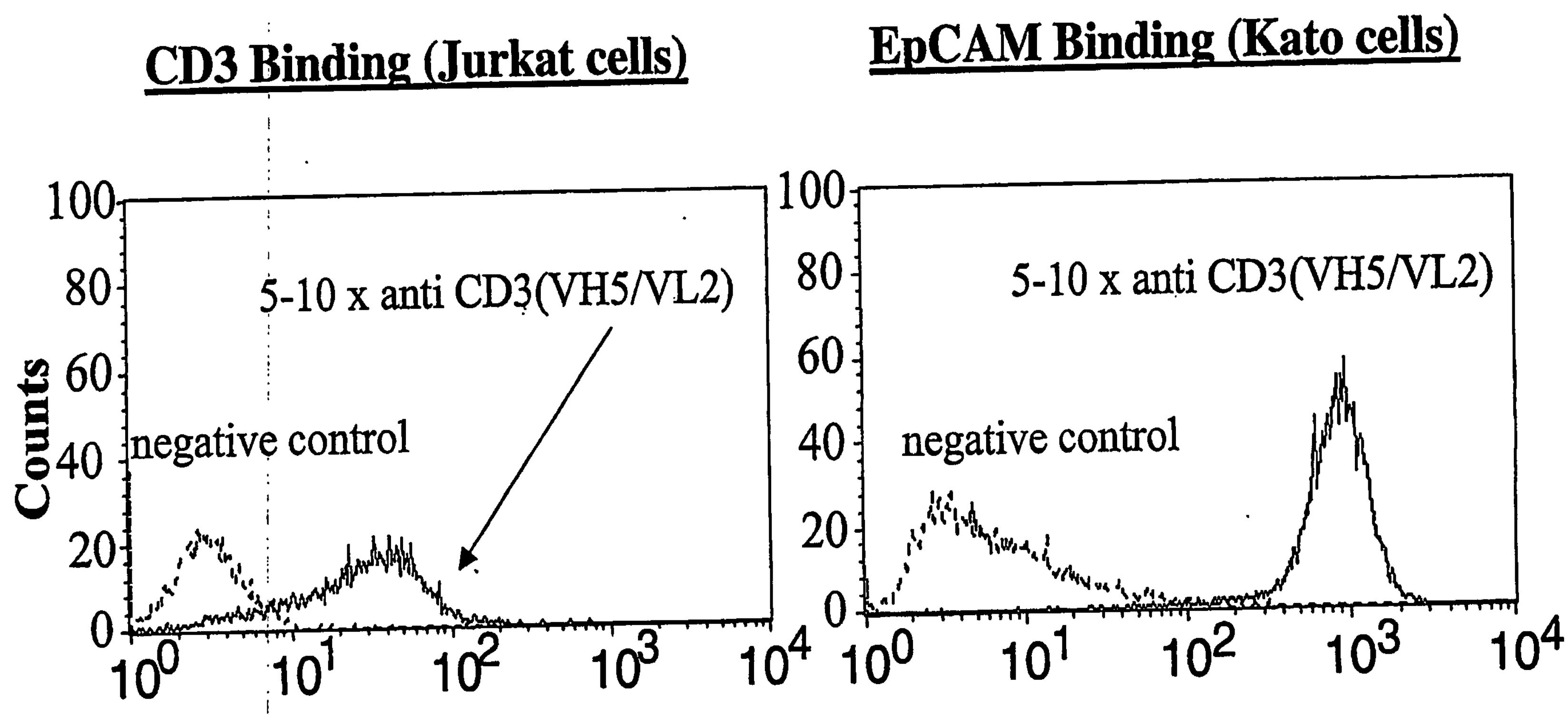
CD3 Binding (Jurkat cells)

EpCAM Binding (Kato cells)



3-1 x
antiCD3(VH5/VL2)
(SEQ ID NO: 49)

Figure 16 B



5-10 x antiCD3(VH5/VL2)
(SEQ ID NO:63)

Figure 17

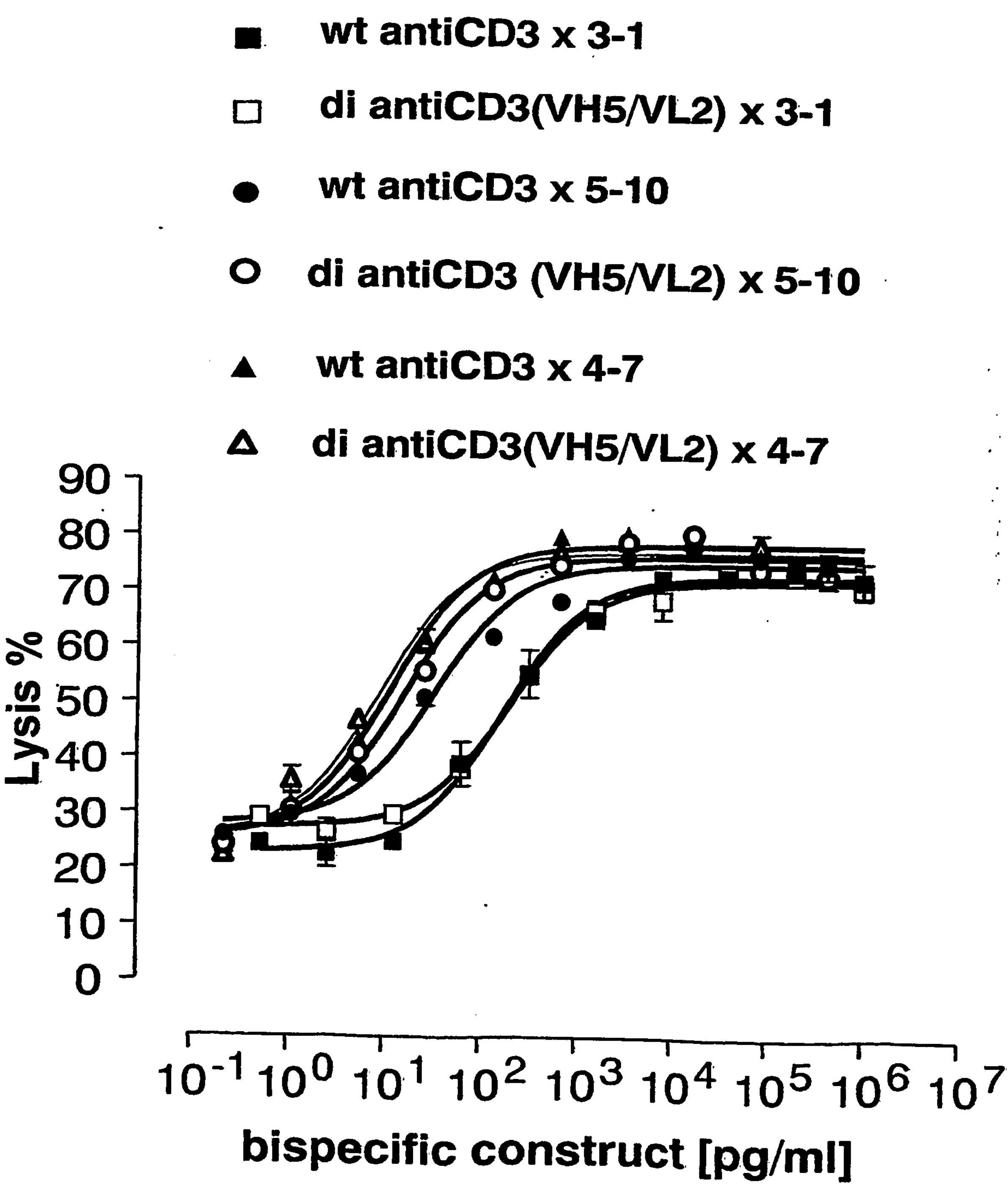
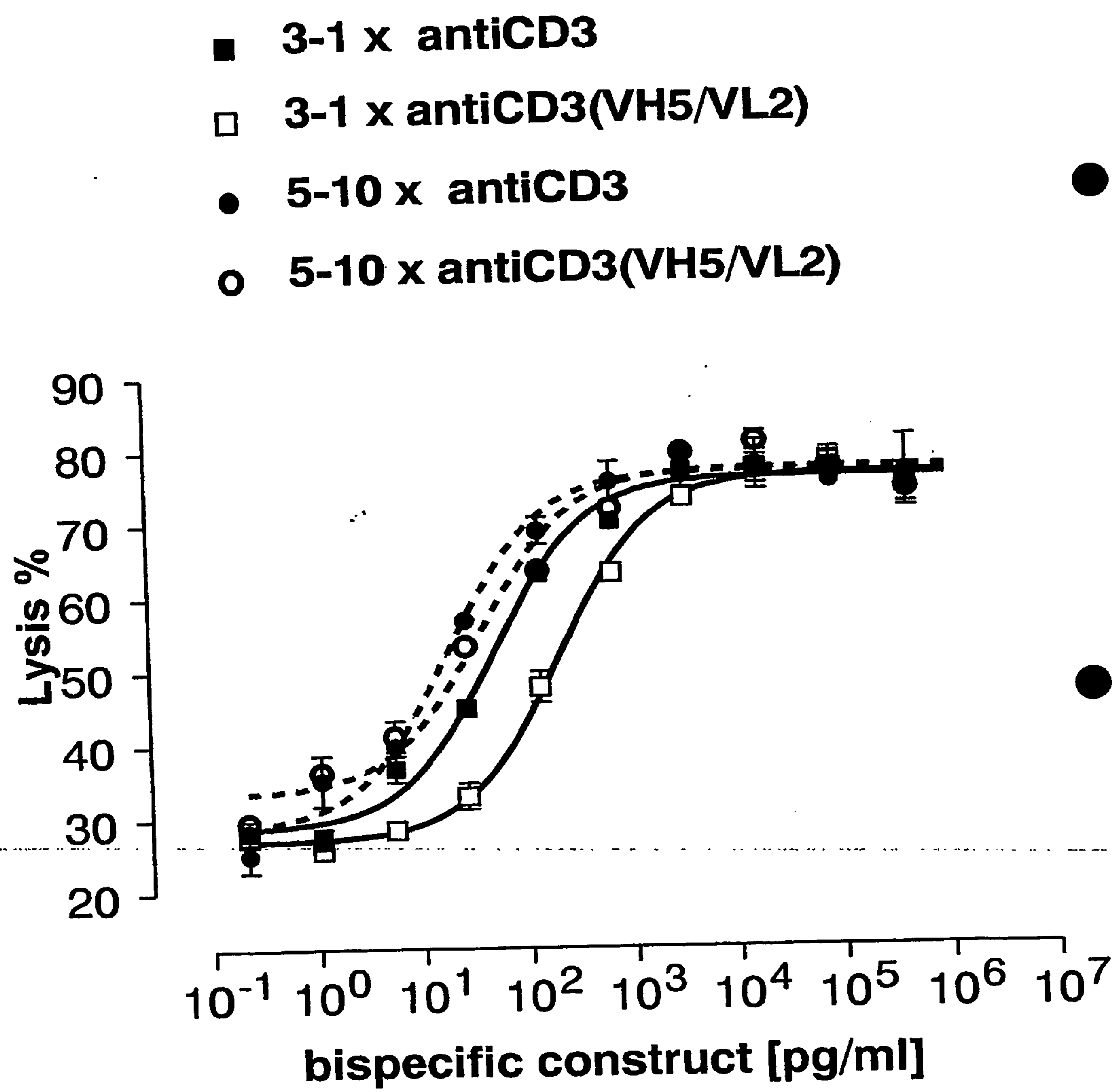

wt antiCD3 x 3-1
di antiCD3(VH5/VL2) x 3-1
wt antiCD3 x 5-10
di antiCD3 (VH5/VL2) x 5-10
wt antiCD3 x 4-7
di antiCD3(VH5/VL2) x 4-7
Lysis %
90
80
70
60
50
40
30
20
10
0
10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4} 10^{5} 10^{6} 10^{7}
bispecific construct [pg/ml]

Figure 18


3-1 x antiCD3
3-1 x antiCD3(VH5/VL2)
5-10 x antiCD3
5-10 x antiCD3(VH5/VL2)
Lysis %
90
80
70
60
50
40
30
20
10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4} 10^{5} 10^{6} 10^{7}
bispecific construct [pg/ml]

SEQUENCE LISTING

<110> Micromet AG

<120> Multispecific deimmunized CD3 binders

<130> G 2728 EP

<160> 409

<170> PatentIn version 3.1

<210> 1
<211> 729
<212> DNA
<213> artificial sequence

<220>
<223> wt Anti-CD3 cassette
<400> 1

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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac     180
aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac     240
atgcaactga gcagcctgac atctgaggac tctgcagtct attactgtgc aagatattat     300
gatgatcatt actgccttga ctactggggc caaggcacca ctctcacagt ctcctcagtc     360
gaaggtggaa gtggaggttc tggtggaagt ggaggttcag gtggagtcga cgacattcag     420
ctgacccagt ctccagcaat catgtctgca tctccagggg agaaggtcac catgacctgc     480
agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagtcagg cacctccccc     540
aaaagatgga tttatgacac atccaaagtg gcttctggag tcccttatcg cttcagtggc     600
agtgggtctg ggacctcata ctctctcaca atcagcagca tggaggctga agatgctgcc     660
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gagctgaaa                                                             729
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<210> 2
<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> wt Anti-CD3 cassette

<400> 2

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Leu Thr Val Ser Ser Val Glu Gly Gly Ser Gly Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Val Asp Asp Ile Gln Leu Thr Gln Ser
130 135 140

Pro Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser
165 170 175

Gly Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser
195 200 205

Leu Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

3

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu
225 230 235 240

Glu Leu Lys

<210> 3

<211> 18

<212> PRT

<213> artificial sequence

<220>

<223> deimmunized linker

<400> 3

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
1 5 10 15

Ala Asp

<210> 4

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH2/VL1

<400> 4

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tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360

gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420

atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480

agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600

agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660

acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720

gagatcaaa 729

<210> 5

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH2/VL1

<400> 5

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
        195   200   205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
    210   215   220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225   230   235   240

Glu Ile Lys

<210> 6

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH2/VL2

<400> 6

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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360

gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420

ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480

agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600

agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660

acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720

gagatcaaa 729

<210> 7

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH2/VL2

<400> 7

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 8

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH2/VL3

<400> 8
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

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ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480

agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600

agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660

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gagatcaaa 729

<210> 9

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH2VL3

<400> 9

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 10

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH3/VL1

<400> 10
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tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240
ctgcaaatga acagcctgaa aactgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaa 729

<210> 11

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH3/VL1

<400> 11

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 12

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH3/VL2

<400> 12

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240
ctgcaaatga acagcctgaa aactgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaa 729

<210> 13

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH3/VL2

<400> 13

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 14

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH3/VL3

<400> 14

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240

ctgcaaatga acagcctgaa aactgaggac actgcagtct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360

gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420

ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480

agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600

agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660

acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720

gagatcaaa 729

<210> 15

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH3/VL3

<400> 15

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
            20   25   30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
    50   55   60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
        115   120   125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
    130   135   140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145   150   155   160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
                165   170   175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
            180   185   190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
        195   200   205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
    210   215   220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225   230   235   240

Glu Ile Lys

<210> 16

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL1

<400> 16

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaa 729

<210> 17

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL1

<400> 17

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 18

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL2

<400> 18
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tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaa 729

<210> 19

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL2

<400> 19

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 20

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL3

<400> 20
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360

gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaa 729

<210> 21

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL3

<400> 21

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 22

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH7/VL1

<400> 22
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaa 729

<210> 23

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH7/VL1

<400> 23

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
    50   55   60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
        115   120   125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
    130   135   140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145   150   155   160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
                165   170   175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
            180   185   190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
        195   200   205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
    210   215   220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 24

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH7/VL2

<400> 24
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaa 729

<210> 25

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH7/VL2

<400> 25

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

22

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 26

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH7/VL3

<400> 26
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360

gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420

ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480

agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600

agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660

acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720

gagatcaaa 729

<210> 27

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH7/VL3

<400> 27

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr

65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 28

<211> 20

<212> DNA

<213> artificial sequence

<220>

<223> Sequencing primer

<400> 28
cctcagacag tggttcaaag 20

<210> 29

<211> 18

<212> DNA

<213> artificial sequence

<220>

<223> Sequencing primer

<400> 29
agccgccacg tgggcctc 18

<210> 30

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 3-1 VHVL

<400> 30
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gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
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gaaaccatta ctattaattg cagggcaagt aagagcatta gcaaatattt agcctggtat 1260

caagagaaac ctgggaaaac taataagctt cttatctact ctggatccac tttgcaatct 1320

ggaattccat caaggttcag tggcagtgga tctggtacag atttcactct caccatcagt 1380

agcctggagc ctgaagattt tgcaatgtat tactgtcaac agcataatga atatccgtac 1440

acgttcggag gggggaccaa gcttgagatc aaa 1473

<210> 31

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 3-1 VHVL

<400> 31

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
275 280 285

Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp Leu Phe Pro Gly
290 295 300

Ser Gly Asn Thr His Tyr Asn Glu Arg Phe Arg Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Phe Met Gln Leu Ser Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
340 345 350

Asp Glu Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
355 360 365

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
370 375 380

Glu Leu Val Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly
385 390 395 400

Glu Thr Ile Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Tyr
405 410 415

Leu Ala Trp Tyr Gln Glu Lys Pro Gly Lys Thr Asn Lys Leu Leu Ile
420 425 430

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ser Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
    450   455   460

Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln His Asn Glu Tyr Pro Tyr
465   470   475   480

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
                485   490

<210> 32

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VHVL

<400> 32

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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac     180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac     240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat     300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc     360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta     420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc     480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc     540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc     600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc     660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg     720
gagatcaaat ccggaggtgg tggatccgag gtgcagctgc tcgagcagtc tggagctgag     780
ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca     840
aactatggtt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag     900
gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg     960
actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac    1020
tctgcggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctggtacttc    1080
gatgtctggg gccaagggac cacggtcacc gtctcctcag gtggtggtgg ttctggcggc    1140
ggcggctccg gtggtggtgg ttctgagctc gtgatgaccc agactccact ctccctgcct    1200
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt    1260
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aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 1320

atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 1380

gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440

tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500

<210> 33

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VHVL

<400> 33

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 34

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VLVH

<400> 34

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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac     180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac     240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat     300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc     360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta     420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc     480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc     540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc     600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc     660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg     720
gagatcaaat ccggaggtgg tggatccgag ctcgtgatga cccagactcc actctccctg     780
cctgtcagtc ttggagatca agcctccatc tcttgcagat ctagtcagag ccttgtacac     840
agtaatggaa acacctattt acattggtac ctgcagaagc caggccagtc tccaaagctc     900
ctgatctaca aagtttccaa ccgattttct ggggtcccag acaggttcag tggcagtgga     960
tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat    1020
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gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260

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cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440

actaactacg actggtactt cgatgtctgg ggccaaggga ccacggtcac cgtctcctca 1500

<210> 35

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VLVH

<400> 35

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr

435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
485 490 495

Thr Val Ser Ser
500

<210> 36

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 5-10 VHVL

<400> 36

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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac     180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac     240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat     300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc     360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta     420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc     480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc     540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc     600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc     660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg     720
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aactactggc taggttgggt aaagcagagg cctggacatg gacttgagtg gattggagat     900
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<210> 37

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 5-10 VHVL

<400> 37

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
                85   90   95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
        115   120   125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
    130   135   140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys

145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Ile Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
275 280 285

Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp Ile Phe Pro Gly
290 295 300

Ser Gly Asn Ile His Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu
325 330 335

Thr Phe Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
340 345 350

Asp Glu Pro Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
355 360 365

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
370 375 380

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
385 390 395 400

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
405 410 415

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
420 425 430

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
435 440 445

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
450 455 460

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
465 470 475 480

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
485 490 495

Lys

<210> 38

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 5-10 VLVH

<400> 38
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgag ctcgtgatga cacagtctcc atcctccctg 780
actgtgacag caggagagaa ggtcactatg agctgcaagt ccagtcagag tctgttaaac 840
agtggaaatc aaaagaacta cttgacctgg taccagcaga aaccagggca gcctcctaaa 900
ctgttgatct actgggcatc cactagggaa tctggggtcc ctgatcgctt cacaggcagt 960

ggatctggaa cagatttcac tctcaccatc agcagtgtgc aggctgaaga cctggcagtt 1020
tattactgtc agaatgatta tagttatccg ctcacgttcg gtgctgggac caagcttgag 1080
atcaaaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgaggtgcag 1140
ctgctcgagc agtctggagc tgagctggta aggcctggga cttcagtgaa gatatcctgc 1200
aaggcttctg gatacgcctt cactaactac tggctaggtt gggtaaagca gaggcctgga 1260
catggacttg agtggattgg agatattttc cctggaagtg gtaatatcca ctacaatgag 1320
aagttcaagg gcaaagccac actgactgca gacaaatctt cgagcacagc ctatatgcag 1380
ctcagtagcc tgacatttga ggactctgct gtctatttct gtgcaagact gaggaactgg 1440
gacgagccta tggactactg gggccaaggg accacggtca ccgtctcctc a 1491

<210> 39

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 5-10 VLVH

<400> 39

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser
245 250 255

Pro Ser Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys
260 265 270

Lys Ser Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu
275 280 285

Thr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
290 295 300

Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser
305 310 315 320

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu
325 330 335

Asp Leu Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr
340 345 350

Phe Gly Ala Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly
355 360 365

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
370 375 380

Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Ile Ser Cys
385 390 395 400

Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
405 410 415

Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp Ile Phe Pro Gly
420 425 430

Ser Gly Asn Ile His Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
435 440 445

Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu
450 455 460

Thr Phe Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
465 470 475 480

Asp Glu Pro Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

Ser

<210> 40
<211> 35
<212> DNA
<213> artificial sequence

<220>
<223> DI anti-CD3 K52VHBsrGI

<400> 40
aggtgtacac tccgacgtcc aactggtgca gtcag 35

<210> 41
<211> 30
<212> DNA
<213> artificial sequence

<220>
<223> DI anti-CD3 52VLBspEI

<400> 41
aatccggatt tgatctccac cttggtcccg 30

<210> 42
<211> 51
<212> DNA
<213> artificial sequence

<220>

<223> 4-7 VH GS15 FOR

<400> 42
ggcggcggcg gctccggtgg tggtggttct gaggtgcagc tgctcgagca g 51

<210> 43

<211> 53

<212> DNA

<213> artificial sequence

<220>

<223> 4-7 VH SalI REV

<400> 43
ttttaagtcg acctaatgat gatgatgatg atgtgaggag acggtgaccg tgg 53

<210> 44

<211> 49

<212> DNA

<213> artificial sequence

<220>

<223> 510VLBspEI

<400> 44
ctgaaatccg gaggtggtgg atccgagctc gtgatgacac agtctccat 49

<210> 45

<211> 53

<212> DNA

<213> artificial sequence

<220>

<223> 510VLGS15REV

<400> 45
ggagccgccg ccgccagaac caccaccacc tttgatctca agcttggtcc cag 53

<210> 46

<211> 49

<212> DNA

<213> artificial sequence

<220>

<223> 510VHGS15

<400> 46
ggcggcggcg gctccggtgg tggtggttct gaggtgcagc tgctcgagc 49

<210> 47

<211> 53

<212> DNA

<213> artificial sequence

<220>

<223> 510VHSalIREV

<400> 47
ttttaagtcg acctaatgat gatgatgatg atgtgaggag acggtgaccg tgg 53

<210> 48

<211> 1518

<212> DNA

<213> artificial sequence

<220>

<223> 3-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 48
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgag 60
ctcgtcatga cccagtctcc atcttatctt gctgcatctc ctggagaaac cattactatt 120
aattgcaggg caagtaagag cattagcaaa tatttagcct ggtatcaaga gaaacctggg 180
aaaactaata agcttcttat ctactctgga tccactttgc aatctggaat tccatcaagg 240
ttcagtggca gtggatctgg tacagatttc actctcacca tcagtagcct ggagcctgaa 300
gattttgcaa tgtattactg tcaacagcat aatgaatatc cgtacacgtt cggaggggggg 360
accaagcttg agatcaaagg tggtggtggt tctggcggcg gcggctccgg tggtggtggt 420
tctgaggtgc agctgctcga gcagtctgga gctgagctgg tgaaacctgg ggcctcagtg 480
aagatatcct gcaaggcttc tggatacgcc ttcactaact actggctagg ttgggtaaag 540
cagaggcctg gacatggact tgagtggatt ggagatcttt tccctggaag tggtaatact 600
cactacaatg agaggttcag gggcaaagcc acactgactg cagacaaatc ctcgagcaca 660
gcctttatgc agctcagtag cctgacatct gaggactctg ctgtctattt ctgtgcaaga 720

ttgaggaact gggacgaggc tatggactac tggggccaag ggaccacggt caccgtctcc 780
tccggaggtg gtggctccga cgtccaactg gtgcagtcag gggctgaagt gaaaaaacct 840
ggggcctcag tgaaggtgtc ctgcaaggct tctggctaca cctttactag gtacacgatg 900
cactgggtaa ggcaggcacc tggacagggt ctggaatgga ttggatacat taatcctagc 960
cgtggttata ctaattacgc agacagcgtc aagggccgct tcacaatcac tacagacaaa 1020
tccaccagca cagcctacat ggaactgagc agcctgcgtt ctgaggacac tgcaacctat 1080
tactgtgcaa gatattatga tgatcattac tgccttgact actggggcca aggcaccacg 1140
gtcaccgtct cctcaggcga aggtactagt actggttctg gaggttcagg tggagcagac 1200
gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 1260
ctgagctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 1320
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 1380
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 1440
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 1500
accaaggtgg agatcaaa 1518

<210> 49

<211> 506

<212> PRT

<213> artificial sequence

<220>

<223> 3-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 49

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Leu Val Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala
20 25 30

Ser Pro Gly Glu Thr Ile Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile
35 40 45

Ser Lys Tyr Leu Ala Trp Tyr Gln Glu Lys Pro Gly Lys Thr Asn Lys
50 55 60

Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ser Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
85 90 95

Leu Glu Pro Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln His Asn Glu
100 105 110

Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln
130 135 140

Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val
145 150 155 160

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu
165 170 175

Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp
180 185 190

Leu Phe Pro Gly Ser Gly Asn Thr His Tyr Asn Glu Arg Phe Arg Gly
195 200 205

Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Phe Met Gln
210 215 220

Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
225 230 235 240

Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
245 250 255

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln
260 265 270

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
275 280 285

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
290 295 300

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
305 310 315 320

Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
325 330 335

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
340 345 350

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
355 360 365

45
His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
370 375 380

Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ala Asp
385 390 395 400

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
405 410 415

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
420 425 430

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
435 440 445

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
450 455 460

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
465 470 475 480

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
485 490 495

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
500 505

<210> 50

<211> 60

<212> DNA

<213> artificial sequence

<220>

<223> Me83

<400> 50
ggttctggcg gcggcggctc cggtggtggt ggttctgagg tgcagctgct cgacagtctg 60

<210> 51

<211> 41

<212> DNA

<213> artificial sequence

<220>

<223> Me84

<400> 51

gtgctccgga ggagacggtg accgtggtcc cttggcccca g 41

<210> 52

<211> 53

<212> DNA

<213> artificial sequence

<220>

<223> Me90

<400> 52
ccggagccgc cgccgccaga accaccacca cctttgatct caagcttggt ccc 53

<210> 53

<211> 52

<212> DNA

<213> artificial sequence

<220>

<223> Me91a

<400> 53
ggattgtaca ctccgagctc gtcatgaccc agtctccatc ttatcttgct gc 52

<210> 54

<211> 1560

<212> DNA

<213> artificial sequence

<220>

<223> 3-5(VL-VH)xanti-CD3 (VH(5)-VL(2))

<400> 54
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgcg 60
cgcgagctcg tgatgaccca gactccactc tccctgcctg tcagtcttgg agatcaagcc 120
tccatctctt gcagatctag tcagagcctt gtacacagta atggaaacac ctatttacat 180
tggtacctgc agaagccagg ccagtctcca aagctcctga tctacaaagt ttccaaccga 240
ttttctgggg tcccagacag gttcagtggc agtggatcag ggacagattt cacactcaag 300
atcagcagag tggaggctga ggatctggga gtttatttct gctctcaaag tacacatgtt 360
ccgtacacgt tcggaggggg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 420
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 480

gtaaggcctg ggacttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaagc 540

tatggtttaa gctgggtgaa gcagagaact ggacagggcc ttgagtggat tggagaggtt 600

tatcctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 660

gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacatc tgaggactct 720

gcggtctatt tctgtgcaag acggggatcc tacggtagta actacgactg gtacttcgat 780

gtctggggcc aagggaccac ggtcaccgtc tcctccggag gtggtggctc cgacgtccaa 840

ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 900

gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 960

ggtctggaat ggattggata cattaatcct agccgtggtt atactaatta cgcagacagc 1020

gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1080

agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1140

tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctcagg cgaaggtact 1200

agtactggtt ctggtggaag tggaggttca ggtggagcag acgacattgt actgacccag 1260

tctccagcaa ctctgtctct gtctccaggg gagcgtgcca ccctgagctg cagagccagt 1320

caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 1380

atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 1440

gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1500

tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1560

<210> 55

<211> 520

<212> PRT

<213> artificial sequence

<220>

<223> 3-5(VL-VH)xanti-CD3 (VH(5)-VL(2))

<400> 55

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1   5   10   15

Val His Ser Ala Arg Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu
            20   25   30

Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln
        35   40   45

Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln
    50   55   60

Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg
65 70 75 80

Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr
100 105 110

Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr
115 120 125

Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu
145 150 155 160

Val Arg Pro Gly Thr Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr
165 170 175

Thr Phe Thr Ser Tyr Gly Leu Ser Trp Val Lys Gln Arg Thr Gly Gln
180 185 190

Gly Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly Asn Ala Tyr
195 200 205

Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser
210 215 220

Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser
225 230 235 240

Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Gly Ser Asn Tyr Asp
245 250 255

Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
260 265 270

Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val
275 280 285

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
290 295 300

Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Gln
305 310 315 320

Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn
325 330 335

49

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser
340 345 350

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
355 360 365

Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp
370 375 380

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr
385 390 395 400

Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile
405 410 415

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
420 425 430

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
435 440 445

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
450 455 460

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
465 470 475 480

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
485 490 495

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
500 505 510

Gly Gly Thr Lys Val Glu Ile Lys
515 520

<210> 56

<211> 40

<212> DNA

<213> artificial sequence

<220>

<223> Me81

<400> 56
ggatgcgcgc gagctcgtga tgacccagac tccactctcc 40

<210> 57

<211> 1545

<212> DNA

<213> artificial sequence

<220>

<223> 4-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 57
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgag 60
ctcgtgatga cacagtctcc atcctccctg agtgtgtcag caggagagaa ggtcactatg 120
agctgcaagt ccagtcagag tctgttaaac agtggaaatc aaaagaacta cttggcctgg 180
taccagcaga aaccagggca gcctcctaaa ctgttgatct acggggcatc cactagggaa 240
tctggggtcc ctgatcgctt cacaggcagt ggatctggaa cagatttcac tctcaccatc 300
agcagtgtgc aggctgaaga cctggcagtt tattactgtc agaatgatta tagttatccg 360
tacacgttcg gaggggggac caagcttgag atcaaaggtg gtggtggttc tggcggcggc 420
ggctccggtg gtggtggttc tgaggtgcag ctgctcgagc agtctggagc tgagctggta 480
aggcctggga cttcagtgaa gatatcctgc aaggcttctg gatacgcctt cactaactac 540
tggctaggtt gggttaagca gaggcctgga catggacttg aatgggttgg agatattttc 600
cctggaagtg gtaatgctca ctacaatgag aagttcaagg gcaaagccac actgactgca 660
gacaagtcct cgtacacagc ctatatgcag ctcagtagcc tgacatctga ggactctgct 720
gtctatttct gtgcaagatt gcggaactgg gacgaggcta tggactactg gggccaaggg 780
accacggtca ccgtctcctc cggaggtggt ggctccgacg tccaactggt gcagtcaggg 840
gctgaagtga aaaaacctgg ggcctcagtg aaggtgtcct gcaaggcttc tggctacacc 900
tttactaggt acacgatgca ctgggtaagg caggcacctg gacagggtct ggaatggatt 960
ggatacatta atcctagccg tggttatact aattacgcag acagcgtcaa gggccgcttc 1020
acaatcacta cagacaaatc caccagcaca gcctacatgg aactgagcag cctgcgttct 1080
gaggacactg caacctatta ctgtgcaaga tattatgatg atcattactg ccttgactac 1140
tggggccaag gcaccacggt caccgtctcc tcaggcgaag gtactagtac tggttctggt 1200
ggaagtggag gttcaggtgg agcagacgac attgtactga cccagtctcc agcaactctg 1260
tctctgtctc caggggagcg tgccaccctg agctgcagag ccagtcaaag tgtaagttac 1320
atgaactggt accagcagaa gccgggcaag gcacccaaaa gatggattta tgacacatcc 1380
aaagtggctt ctggagtccc tgctcgcttc agtggcagtg ggtctgggac cgactactct 1440
ctcacaatca acagcttgga ggctgaagat gctgccactt attactgcca acagtggagt 1500
agtaacccgc tcacgttcgg tggcgggacc aaggtggaga tcaaa 1545

<210> 58

<211> 515

<212> PRT

<213> artificial sequence

<220>

<223> 4-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 58

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val
20 25 30

Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu
35 40 45

Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys
50 55 60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu
65 70 75 80

Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe
85 90 95

Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
100 105 110

Cys Gln Asn Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
115 120 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val
145 150 155 160

Arg Pro Gly Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala
165 170 175

Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly
180 185 190

Leu Glu Trp Val Gly Asp Ile Phe Pro Gly Ser Gly Asn Ala His Tyr
195 200 205

Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser
210 215 220

Tyr Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala

225 230 235 240

Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr
245 250 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
260 265 270

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
275 280 285

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
290 295 300

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
305 310 315 320

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
325 330 335

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
340 345 350

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
355 360 365

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
370 375 380

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
385 390 395 400

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
405 410 415

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
420 425 430

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
435 440 445

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
450 455 460

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
465 470 475 480

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
485 490 495

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
500 505 510

Glu Ile Lys
515

<210> 59

<211> 44

<212> DNA

<213> artificial sequence

<220>

<223> Me92a

<400> 59
ggattgtaca ctccgagctc gtgatgacac agtctccatc ctcc 44

<210> 60

<211> 1560

<212> DNA

<213> artificial sequence

<220>

<223> 4-7(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 60
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgcg 60
cgcgagctcg tgatgaccca gactccactc tccctgcctg tcagtcttgg agatcaagcc 120
tccatctctt gcagatctag tcagagcctt gtacacagta atggaaacac ctatttacat 180
tggtacctgc agaagccagg ccagtctcca aagctcctga tctacaaagt ttccaaccga 240
ttttctgggg tcccagacag gttcagtggc agtggatcag ggacagattt cacactcaag 300
atcagcagag tggaggctga ggatctggga gtttatttct gctctcaaag tacacatgtt 360
ccgtacacgt tcggaggggg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 420
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 480
gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaaac 540
tatggtttaa gctgggtgaa gcagaggcct ggacaggtcc ttgagtggat tggagaggtt 600
tatcctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 660
gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct 720
gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat 780
gtctggggcc aagggaccac ggtcaccgtc tcctccggag gtggtggctc cgacgtccaa 840
ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 900

gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 960

ggtctggaat ggattggata cattaatcct agccgtggtt atactaatta cgcagacagc 1020

gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1080

agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1140

tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctcagg cgaaggtact 1200

agtactggtt ctggtggaag tggaggttca ggtggagcag acgacattgt actgacccag 1260

tctccagcaa ctctgtctct gtctccaggg gagcgtgcca ccctgagctg cagagccagt 1320

caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 1380

atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 1440

gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1500

tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1560

<210> 61

<211> 520

<212> PRT

<213> artificial sequence

<220>

<223> 4-7(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 61

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1   5   10   15

Val His Ser Ala Arg Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu
            20   25   30

Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln
        35   40   45

Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln
    50   55   60

Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg
65   70   75   80

Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                85   90   95

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr
            100   105   110

Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr
        115   120   125

Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu
145 150 155 160

Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr
165 170 175

Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg Pro Gly Gln
180 185 190

Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly Asn Ala Tyr
195 200 205

Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser
210 215 220

Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser
225 230 235 240

Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr Asn Tyr Asp
245 250 255

Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
260 265 270

Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val
275 280 285

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
290 295 300

Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Gln
305 310 315 320

Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn
325 330 335

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser
340 345 350

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
355 360 365

Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp
370 375 380

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr
385 390 395 400

Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile
405 410 415

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
420 425 430

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
435 440 445

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
450 455 460

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
465 470 475 480

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
485 490 495

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
500 505 510

Gly Gly Thr Lys Val Glu Ile Lys
515 520

<210> 62

<211> 1545

<212> DNA

<213> artificial sequence

<220>

<223> 5-10(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 62
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgag 60

ctcgtgatga cacagtctcc atcctccctg actgtgacag caggagagaa ggtcactatg 120

agctgcaagt ccagtcagag tctgttaaac agtggaaatc aaaagaacta cttgacctgg 180

taccagcaga aaccagggca gcctcctaaa ctgttgatct actgggcatc cactagggaa 240

tctggggtcc ctgatcgctt cacaggcagt ggatctggaa cagatttcac tctcaccatc 300

agcagtgtgc aggctgaaga cctggcagtt tattactgtc agaatgatta tagttatccg 360

ctcacgttcg gtgctgggac caagcttgag atcaaaggtg gtggtggttc tggcggcggc 420

ggctccggtg gtggtggttc tgaggtgcag ctgctcgagc agtctggagc tgagctggta 480

aggcctggga cttcagtgaa gatatcctgc aaggcttctg gatacgcctt cactaactac 540

tggctaggtt gggtaaagca gaggcctgga catggacttg agtggattgg agatattttc 600

cctggaagtg gtaatatcca ctacaatgag aagttcaagg gcaaagccac actgactgca 660

gacaaatctt cgagcacagc ctatatgcag ctcagtagcc tgacatttga ggactctgct 720

gtctatttct gtgcaagact gaggaactgg gacgagccta tggactactg gggccaaggg 780

accacggtca ccgtctcctc cggaggtggt ggctccgacg tccaactggt gcagtcaggg 840

gctgaagtga aaaaacctgg ggcctcagtg aaggtgtcct gcaaggcttc tggctacacc 900

tttactaggt acacgatgca ctgggtaagg caggcacctg gacagggtct ggaatggatt 960

ggatacatta atcctagccg tggttatact aattacgcag acagcgtcaa gggccgcttc 1020

acaatcacta cagacaaatc caccagcaca gcctacatgg aactgagcag cctgcgttct 1080

gaggacactg caacctatta ctgtgcaaga tattatgatg atcattactg ccttgactac 1140

tggggccaag gcaccacggt caccgtctcc tcaggcgaag gtactagtac tggttctggt 1200

ggaagtggag gttcaggtgg agcagacgac attgtactga cccagtctcc agcaactctg 1260

tctctgtctc caggggagcg tgccaccctg agctgcagag ccagtcaaag tgtaagttac 1320

atgaactggt accagcagaa gccgggcaag gcacccaaaa gatggattta tgacacatcc 1380

aaagtggctt ctggagtccc tgctcgcttc agtggcagtg ggtctgggac cgactactct 1440

ctcacaatca acagcttgga ggctgaagat gctgccactt attactgcca acagtggagt 1500

agtaacccgc tcacgttcgg tggcgggacc aaggtggaga tcaaa 1545

<210> 63

<211> 515

<212> PRT

<213> artificial sequence

<220>

<223> 5-10(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 63

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val
20 25 30

Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu
35 40 45

Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys
50 55 60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu
65 70 75 80

Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe

85 90 95

Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
100 105 110

Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys
115 120 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val
145 150 155 160

Arg Pro Gly Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala
165 170 175

Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly
180 185 190

Leu Glu Trp Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr
195 200 205

Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser
210 215 220

Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala
225 230 235 240

Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr
245 250 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
260 265 270

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
275 280 285

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
290 295 300

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
305 310 315 320

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
325 330 335

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
340 345 350

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
355 360 365

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
370 375 380

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
385 390 395 400

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
405 410 415

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
420 425 430

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
435 440 445

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
450 455 460

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
465 470 475 480

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
485 490 495

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
500 505 510

Glu Ile Lys
515

<210> 64

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL2x3-5

<400> 64

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360

gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
ctggtaaggc ctgggacttc agtgaagctg tcctgcaagg cttctggcta caccttcaca 840
agctatggtt taagctgggt gaagcagaga actggacagg gccttgagtg gattggagag 900
gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960
actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac atctgaggac 1020
tctgcggtct atttctgtgc aagacgggga tcctacggta gtaactacga ctggtacttc 1080
gatgtctggg gccaagggac cacggtcacc gtctcctcag gtggtggtgg ttctggcggc 1140
ggcggctccg gtggtggtgg ttctgagctc gtgatgaccc agactccact ctccctgcct 1200
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260
aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 1320
atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 1380
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440
tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500

<210> 65

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL2x3-5

<400> 65

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Thr Gly Gln Gly Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Gly Ser Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 66

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL2x4-1

<400> 66
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
ctggtaaggc ctgggacttc agtgaagata tcctgcaagg cttctggata cgccttcact 840
aactactggc taggttgggt taagcagagg cctggacatg gacttgaatg ggttggagat 900
attttccctg gaagtggtaa tgctcactac aatgagaagt tcaagggcaa agccacactg 960
actgcagaca agtcctcgta cacagcctat atgcagctca gtagcctgac atctgaggac 1020
tctgctgtct atttctgtgc aagattgcgg aactgggacg aggctatgga ctactggggc 1080
caagggacca cggtcaccgt ctcctcaggt ggtggtggtt ctggcggcgg cggctccggt 1140
ggtggtggtt ctgagctcgt gatgacacag tctccatcct ccctgagtgt gtcagcagga 1200
gagaaggtca ctatgagctg caagtccagt cagagtctgt taaacagtgg aaatcaaaag 1260
aactacttgg cctggtacca gcagaaacca gggcagcctc ctaaactgtt gatctacggg 1320
gcatccacta gggaatctgg ggtccctgat cgcttcacag gcagtggatc tggaacagat 1380
ttcactctca ccatcagcag tgtgcaggct gaagacctgg cagtttatta ctgtcagaat 1440
gattatagtt atccgtacac gttcggaggg gggaccaagc ttgagatcaa a 1491

<210> 67

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL2x4-1

<400> 67

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Ile Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
275 280 285

Gln Arg Pro Gly His Gly Leu Glu Trp Val Gly Asp Ile Phe Pro Gly
290 295 300

Ser Gly Asn Ala His Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

65

Thr Ala Asp Lys Ser Ser Tyr Thr Ala Tyr Met Gln Leu Ser Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
340 345 350

Asp Glu Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
355 360 365

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
370 375 380

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
385 390 395 400

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
405 410 415

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
420 425 430

Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu Ser Gly Val
435 440 445

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
450 455 460

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
465 470 475 480

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
485 490 495

Lys

<210> 68

<211> 18

<212> PRT

<213> artificial sequence

<220>

<223> non-deimmunized linker sequence

<400> 68

Val Glu Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
1 5 10 15

Val Asp

<210> 69

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH2

<400> 69
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 357

<210> 70

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH2

<400> 70

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 71

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH3

<400> 71
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240

ctgcaaatga acagcctgaa aactgaggac actgcagtct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 357

<210> 72

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH3

<400> 72

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 73

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5

<400> 73
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 357

<210> 74

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5

<400> 74

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

69
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 75

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH7

<400> 75
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 357

<210> 76

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH7

<400> 76

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

70

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 77

<211> 318

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VL1

<400> 77

gacattcaga tgacccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc 60

atcacctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120

aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaa 318

<210> 78

<211> 106

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VL1

<400> 78

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
            20   25   30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
        35   40   45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 79

<211> 318

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VL2

<400> 79
gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60

ctgagctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120

aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaa 318

<210> 80

<211> 106

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VL2

<400> 80

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 81

<211> 318

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VL3

<400> 81
gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
ctgacctgca gagccagttc aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaa 318

<210> 82

<211> 106

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VL3

<400> 82

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 83

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR1 anti-CD3 wt

<400> 83
ggctacacct ttactaggta cacgatgcac 30

<210> 84

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR1 anti-CD3 wt

<400> 84

Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
1   5   10

<210> 85

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR1 VH2,3

<400> 85
ggctacaccg ctactaggta cacgatgcac 30

<210> 86

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR1 VH2,3

<400> 86

Gly Tyr Thr Ala Thr Arg Tyr Thr Met His
1   5   10

<210> 87

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR1 VH5,7

<400> 87
ggctacacct ttactaggta cacgatgcac 30

<210> 88

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR1 VH5,7

<400> 88

Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
1 5 10

<210> 89

<211> 51

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR2 wt anti-CD3 VH7

<400> 89
tacattaatc ctagccgtgg ttatactaat tacaatcaga agttcaagga c 51

<210> 90

<211> 17

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR2 wt anti-CD3 VH7

<400> 90

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 91

<211> 51

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR2 VH5

<400> 91
tacattaatc ctagccgtgg ttatactaat tacgcagaca gcgtcaaggg c 51

<210> 92

<211> 17

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR2 VH5

<400> 92

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 93

<211> 51

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR2 VH2,3

<400> 93
tacattaatc ctagccgtgg ttatactaat tacgcacaga agttgcaggg c 51

<210> 94

<211> 17

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR2 VH2,3

<400> 94

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> 95

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR3 wt anti-CD3 VH2,3,5,7

<400> 95
tattatgatg atcattactg ccttgactac 30

<210> 96

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR3 wt anti-CD3 VH2,3,5,7

<400> 96

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 97

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vK CDR1 wt anti-CD3 VL3

<400> 97
agagccagtt caagtgtaag ttacatgaac 30

<210> 98

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vK CDR1 wt anti-CD3 VL3

<400> 98

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
1 5 10

<210> 99

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vK CDR1 VL 1,2

<400> 99
agagccagtc aaagtgtaag ttacatgaac 30

<210> 100

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vK CDR1 VL 1,2

<400> 100

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
1 5 10

<210> 101

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> vK CDR2 wt anti-CD3 VL1-3

<400> 101
gacacatcca aagtggcttc t 21

<210> 102

<211> 7

<212> PRT

<213> artificial sequence

<220>

<223> vK CDR2 wt anti-CD3 VL1-3

<400> 102

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Asp Thr Ser Lys Val Ala Ser
1               5
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<210> 103

<211> 27

<212> DNA

<213> artificial sequence

<220>

<223> vK CDR3 wt anti-CD3 VL1-3

<400> 103
caacagtgga gtagtaaccc gctcacg 27

<210> 104

<211> 9

<212> PRT

<213> artificial sequence

<220>

<223> vK CDR3 wt anti-CD3 VL1-3

<400> 104

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Gln Gln Trp Ser Ser Asn Pro Leu Thr
1               5
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<210> 105

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> vH anti-CD3 with the mutations of cys->ser

<400> 105
gatatcaaac tgcagcagtc aggggctgaa ctggcaagac ctggggcctc agtgaagatg 60
tcctgcaaga cttctggcta cacctttact aggtacacga tgcactgggt aaaacagagg 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac 240
atgcaactga gcagcctgac atctgaggac tctgcagtct attactgtgc aagatattat 300
gatgatcatt actcccttga ctactggggc caaggcacca ctctcacagt ctcctca 357

<210> 106

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> vH anti-CD3 with the mutations of cys ->ser

<400> 106

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Leu Thr Val Ser Ser
115

<210> 107

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR3 anti-CD3 with the mutation cys-> ser

<400> 107
tattatgatg atcattactc ccttgactac 30

<210> 108

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR3 anti-CD3 with the mutation cys-> ser

<400> 108

Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
1 5 10

<210> 109

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> wild type anti-CD3 VH

<400> 109
gatatcaaac tgcagcagtc aggggctgaa ctggcaagac ctggggcctc agtgaagatg 60

tcctgcaaga cttctggcta cacctttact aggtacacga tgcactgggt aaaacagagg 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac 240

atgcaactga gcagcctgac atctgaggac tctgcagtct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca ctctcacagt ctcctca 357

<210> 110

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> wild type anti-CD3 VH

<400> 110

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1   5   10   15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
    50   55   60

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Thr Leu Thr Val Ser Ser
        115

<210> 111

<211> 318

<212> DNA

<213> artificial sequence

<220>

<223> wild type anti-CD3 VK

<400> 111

gacattcagc tgacccagtc tccagcaatc atgtctgcat ctccagggga gaaggtcacc 60

atgacctgca gagccagttc aagtgtaagt tacatgaact ggtaccagca gaagtcaggc 120

acctccccca aaagatggat ttatgacaca tccaaagtgg cttctggagt cccttatcgc 180

ttcagtggca gtgggtctgg gacctcatac tctctcacaa tcagcagcat ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtgctggg 300

accaagctgg agctgaaa 318

<210> 112

<211> 106

<212> PRT

<213> artificial sequence

<220>

<223> wild type anti-CD3 VK

<400> 112

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1   5   10   15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
            20   25   30

Asn Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
        35   40   45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Tyr Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
            100   105

<210> 113

<211> 372

<212> DNA

<213> artificial sequence

<220>

<223> CD19 VH

<400> 113

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60

tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120

cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180

aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240

atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300

actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360

accgtctcct cc 372

<210> 114

<211> 124

<212> PRT

<213> artificial sequence

<220>

<223> CD19 VH

<400> 114

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 115

<211> 333

<212> DNA

<213> artificial sequence

<220>

<223> CD19 VL

<400> 115

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaa 333

<210> 116

<211> 111

<212> PRT

<213> artificial sequence

<220>

<223> CD19 VL

<400> 116

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 117

<211> 47

<212> DNA

<213> artificial sequence

<220>

<223> 4-7 VL BspEI FOR

<400> 117

ctgaaatccg gaggtggtgg atccgagctc gtgatgaccc agactcc 47

<210> 118

<211> 52

<212> DNA

<213> artificial sequence

<220>

<223> 4-7 VL GS15 REV

<400> 118
ggagccgccg ccgccagaac caccaccacc tttgatctca agcttggtcc cc 52

<210> 119

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M1 mutant

<400> 119

His Tyr Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 120

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M4 mutant

<400> 120

Tyr Ser Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 121

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M7 mutant

<400> 121

Tyr Tyr Asp Ala His Tyr Cys Leu Asp Tyr
1 5 10

<210> 122

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M9 mutant

<400> 122

Tyr Tyr Asp Asp Gln Tyr Cys Leu Asp Tyr
1 5 10

<210> 123

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M10 mutant

<400> 123

Tyr Tyr Asp Asp Pro Tyr Cys Leu Asp Tyr
1 5 10

<210> 124

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M11 mutant

<400> 124

Tyr Phe Asn Asp His Tyr Cys Leu Asp Tyr

1 5 10

<210> 125

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M13 mutant

<400> 125

Tyr Tyr Asn Asp Gln Tyr Cys Leu Asp Tyr
1 5 10

<210> 126

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M20 mutant

<400> 126

Tyr His Asp Asp Pro Tyr Cys Leu Asp Tyr
1 5 10

<210> 127

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M76 mutant

<400> 127

Tyr Tyr Asp Asp Asn Tyr Cys Leu Asp Tyr
1 5 10

<210> 128

<211> 354

<212> DNA

<213> artificial sequence

<220>

<223> CCR5 Heavy chain

<400> 128
cagctggagc agtctggacc tgaactgaag aagcctggag agacagtcac gatctcctgc 60

aaggcttctg ggtatacctt cacgaagttc ggaatgaact gggtgaagca ggctccagga 120

aagggtttaa agtggatggg ctggatacac acctccactg gagagccaac atattctgat 180

gacttcaagg gacggtttgc cttctctttg gaaacgtctg ccagcactgc ctatttgcgg 240

atcaacaacc tcaaaaatga ggacatggct aaatacttct gtgccagagg tggtccttac 300

gtaaggggtg ctttggacta ctggggtcaa ggaacctcag tcaccgtctc ctcc 354

<210> 129

<211> 118

<212> PRT

<213> artificial sequence

<220>

<223> CCR5 Heavy chain

<400> 129

Gln Leu Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val
1 5 10 15

Thr Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met
20 25 30

Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp
35 40 45

Ile His Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly
50 55 60

Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg
65 70 75 80

Ile Asn Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg
85 90 95

Gly Gly Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ser Val Thr Val Ser Ser
115

<210> 130

<211> 333

<212> DNA

<213> artificial sequence

<220>

<223> CCR5 Light chain

<400> 130

gacattatcc tgatccaatc tccaccttct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac 120

caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc 180

ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240

cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300

acgttcggtg gaggcaccaa gctggaaatc aaa 333

<210> 131

<211> 111

<212> PRT

<213> artificial sequence

<220>

<223> CCR5 Light chain

<400> 131

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 132

<211> 360

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM5-10 heavy chain

<400> 132

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gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag      60
atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag     120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac     180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc     240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg     300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca     360
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<210> 133

<211> 120

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM5-10 heavy chain

<400> 133

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe

85 90 92 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 134

<211> 339

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM5-10 light chain

<400> 134

gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60

atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120

tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgctcacgt tcggtgctgg gaccaagctt gagatcaaa 339

<210> 135

<211> 113

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 5-10 light chain

<400> 135

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 136

<211> 360

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 3-1 VH

<400> 136
gaggtgcagc tgctcgagca gtctggagct gagctggtga aacctggggc ctcagtgaag 60

atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120

aggcctggac atggacttga gtggattgga gatcttttcc ctggaagtgg taatactcac 180

tacaatgaga ggttcagggg caaagccaca ctgactgcag acaaatcctc gagcacagcc 240

tttatgcagc tcagtagcct gacatctgag gactctgctg tctatttctg tgcaagattg 300

aggaactggg acgaggctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360

<210> 137

<211> 120

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 3-1 VH

<400> 137

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Lys Pro Gly
1 5 10 15

Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Leu Phe Pro Gly Ser Gly Asn Thr His Tyr Asn Glu Arg
50 55 60

Phe Arg Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Phe Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 138

<211> 321

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 3-1 VL

<400> 138
gagctcgtca tgacccagtc tccatcttat cttgctgcat ctcctggaga aaccattact 60

attaattgca gggcaagtaa gagcattagc aaatatttag cctggtatca agagaaacct 120

gggaaaacta ataagcttct tatctactct ggatccactt tgcaatctgg aattccatca 180

aggttcagtg gcagtggatc tggtacagat ttcactctca ccatcagtag cctggagcct 240

gaagattttg caatgtatta ctgtcaacag cataatgaat atccgtacac gttcggaggg 300

gggaccaagc ttgagatcaa a 321

<210> 139

<211> 107

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 3-1 VL

<400> 139

95

Glu Leu Val Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly
1   5   10   15

Glu Thr Ile Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Tyr
            20   25   30

Leu Ala Trp Tyr Gln Glu Lys Pro Gly Lys Thr Asn Lys Leu Leu Ile
        35   40   45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65   70   75   80

Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln His Asn Glu Tyr Pro Tyr
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 140

<211> 372

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 3-5 VH

<400> 140
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
ctgtcctgca aggcttctgg ctacaccttc acaagctatg gtttaagctg ggtgaagcag 120
agaactggac agggccttga gtggattgga gaggtttatc ctagaattgg taatgcttac 180
tacaatgaga agttcaaggg caaggccaca ctgactgcag acaaatcctc cagcacagcg 240
tccatggagc tccgcagcct gacatctgag gactctgcgg tctatttctg tgcaagacgg 300
ggatcctacg gtagtaacta cgactggtac ttcgatgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 141

<211> 124

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 3-5 VH

<400> 141

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser
20 25 30

Tyr Gly Leu Ser Trp Val Lys Gln Arg Thr Gly Gln Gly Leu Glu Trp
35 40 45

Ile Gly Glu Val Tyr Pro Arg Ile Gly Asn Ala Tyr Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Ser Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Arg Gly Ser Tyr Gly Ser Asn Tyr Asp Trp Tyr Phe Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 142

<211> 336

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 3-5 VL

<400> 142

gagctcgtga tgacccagac tccactctcc ctgcctgtca gtcttggaga tcaagcctcc 60

atctcttgca gatctagtca gagccttgta cacagtaatg gaaacaccta tttacattgg 120

tacctgcaga agccaggcca gtctccaaag ctcctgatct acaaagtttc caaccgattt 180

tctggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc 240

agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttccg 300

tacacgttcg gaggggggac caagcttgag atcaaa 336

<210> 143

<211> 112

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 3-5 VL

<400> 143

Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1   5   10   15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
            20   25   30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35   40   45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50   55   60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65   70   75   80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
                85   90   95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100   105   110

<210> 144

<211> 360

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 4-1 VH

<400> 144

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60

atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggttaagcag 120

aggcctggac atggacttga atgggttgga gatattttcc ctggaagtgg taatgctcac 180

tacaatgaga agttcaaggg caaagccaca ctgactgcag acaagtcctc gtacacagcc 240

tatatgcagc tcagtagcct gacatctgag gactctgctg tctatttctg tgcaagattg 300

cggaactggg acgaggctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360

<210> 145

<211> 120

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 4-1 VH

<400> 145

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Val Gly Asp Ile Phe Pro Gly Ser Gly Asn Ala His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Tyr Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 146

<211> 339

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 4-1 VL

<400> 146
gagctcgtga tgacacagtc tccatcctcc ctgagtgtgt cagcaggaga gaaggtcact 60

atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttggcc 120

tggtaccagc agaaaccagg gcagcctcct aaactgttga tctacggggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgtacacgt tcggaggggg gaccaagctt gagatcaaa 339

<210> 147

<211> 113

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 4-1 VL

<400> 147

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 148

<211> 372

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 4-7 VH

<400> 148

gaggtgcagc tgctcgagca gtctggagct gagctggcga ggcctggggc ttcagtgaag 60
ctgtcctgca aggcttctgg ctacaccttc acaaactatg gtttaagctg ggtgaagcag 120
aggcctggac aggtccttga gtggattgga gaggtttatc ctagaattgg taatgcttac 180
tacaatgaga agttcaaggg caaggccaca ctgactgcag acaaatcctc cagcacagcg 240
tccatggagc tccgcagcct gacctctgag gactctgcgg tctatttctg tgcaagacgg 300
ggatcctacg atactaacta cgactggtac ttcgatgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 149

<211> 124

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 4-7 VH

<400> 149

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly
1 5 10 15

Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn
20 25 30

Tyr Gly Leu Ser Trp Val Lys Gln Arg Pro Gly Gln Val Leu Glu Trp
35 40 45

Ile Gly Glu Val Tyr Pro Arg Ile Gly Asn Ala Tyr Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Ser Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Arg Gly Ser Tyr Asp Thr Asn Tyr Asp Trp Tyr Phe Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 150

<211> 336

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 4-7 VL

<400> 150

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gagctcgtga tgacccagac tccactctcc ctgcctgtca gtcttggaga tcaagcctcc      60
atctcttgca gatctagtca gagccttgta cacagtaatg gaaacaccta tttacattgg     120
tacctgcaga agccaggcca gtctccaaag ctcctgatct acaaagtttc caaccgattt     180
tctggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc     240
agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttccg     300
tacacgttcg gaggggggac caagcttgag atcaaa                              336
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<210> 151

<211> 112

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 4-7 VL

<400> 151

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Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1               5                   10                  15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
                85                  90                  95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
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<210> 152

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> VH5 Framework 1

<400> 152

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 153

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> VH7 Framework 1

<400> 153

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 154

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> VH2 Framework 1

<400> 154

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 155

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> VH3 Framework 1

<400> 155

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 156

<211> 15

<212> PRT

<213> artificial sequence

<220>

<223> VH5 Framework 2

<400> 156

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
1 5 10 15

<210> 157

<211> 15

<212> PRT

<213> artificial sequence

<220>

<223> VH7 Framework 2

<400> 157

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
1 5 10 15

<210> 158

<211> 22

<212> PRT

<213> artificial sequence

<220>

<223> VH2 Framework 2

<400> 158

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
1   5   10   15

Asn Pro Ser Arg Gly Tyr
            20

<210> 159

<211> 22

<212> PRT

<213> artificial sequence

<220>

<223> VH3 Framework 2

<400> 159

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
1   5   10   15

Asn Pro Ser Arg Gly Tyr
            20

<210> 160

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> VH5 Framework 3

<400> 160

Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
1   5   10   15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
            20   25   30

<210> 161

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> VH7 Framework 3

<400> 161

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> 162

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> VH2 Framework 3

<400> 162

Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
20 25 30

<210> 163

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> VH3 Framework 3

<400> 163

Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu Gln
1 5 10 15

Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> 164

<211> 11

<212> PRT

<213> artificial sequence

<220>

<223> VH5 Framework 4

<400> 164

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
1   5   10

<210> 165

<211> 11

<212> PRT

<213> artificial sequence

<220>

<223> VH7 Framework 4

<400> 165

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
1   5   10

<210> 166

<211> 11

<212> PRT

<213> artificial sequence

<220>

<223> VH2 Framework 4

<400> 166

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
1   5   10

<210> 167

<211> 11

<212> PRT

<213> artificial sequence

<220>

<223> VH3 Framework 4

<400> 167

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
1 5 10

<210> 168

<211> 15

<212> PRT

<213> artificial sequence

<220>

<223> Standard linker

<400> 168

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 169

<211> 366

<212> DNA

<213> artificial sequence

<220>

<223> CD20VH

<400> 169
caggtgcaac tgcggcagcc tggggctgag ctggtgaagc ctggggcctc agtgaagatg 60

tcctgcaagg cttctggcta cacatttacc agttacaata tgcactgggt aaagcagaca 120

cctggacagg gcctggaatg gattggagct atttatccag gaaatggtga tacttcctac 180

aatcagaagt tcaaaggcaa ggccacattg actgcagaca aatcctccag cacagcctac 240

atgcagctca gcagtctgac atctgaggac tctgcggtct attactgtgc aagatcgcac 300

tacggtagta actacgtaga ctactttgac tactggggcc aaggcacact agtcacagtc 360

tcgaca 366

<210> 170

<211> 122

<212> PRT

<213> artificial sequence

<220>

<223> CD20VH

<400> 170

Gln Val Gln Leu Arg Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
    50   55   60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
            100   105   110

Gly Gln Gly Thr Leu Val Thr Val Ser Thr
        115   120

<210> 171

<211> 318

<212> DNA

<213> artificial sequence

<220>

<223> CD20VL

<400> 171

caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca 60

atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga 120

tcctccccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gacctcttac tctctcacaa tcagcagagt ggaggctgaa 240

gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300

acaaaggtgg aaataaaa 318

<210> 172

<211> 106

<212> PRT

<213> artificial sequence

<220>

<223> CD20VL

<400> 172

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Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1               5                   10                  15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
        35                  40                  45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50                  55                  60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65                  70                  75                  80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
                85                  90                  95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys
            100                 105
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<210> 173

<211> 15

<212> DNA

<213> artificial sequence

<220>

<223> GGGGS linker

<400> 173
ggaggtggtg gatcc 15

<210> 174

<211> 5

<212> PRT

<213> artificial sequence

<220>

<223> GGGGS linker

<400> 174

Gly Gly Gly Gly Ser
1   5

<210> 175

<211> 18

<212> DNA

<213> artificial sequence

<220>

<223> SGGGGS linker

<400> 175
tccggaggtg gtggatcc 18

<210> 176

<211> 6

<212> PRT

<213> artificial sequence

<220>

<223> SGGGGS linker

<400> 176

Ser Gly Gly Gly Gly Ser
1   5

<210> 177

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL1

<400> 177
gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780
cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaca gaagttgcag 960
ggccgcgtca caatgactac agacacttcc accagcacag cctacatgga actgagcagc 1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc 1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttcagatgac ccagtctcca 1200
tctagcctgt ctgcatctgt cggggaccgt gtcaccatca cctgcagagc cagtcaaagt 1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
caccatcatc attagagatc tgtcgac 1527

<210> 178

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL1

<400> 178

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro
385 390 395 400

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 179

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL2

<400> 179

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gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc      60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac     120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct     180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat     240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg     300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc     360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct     420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg     480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga     540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa     600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat     660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg     720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg     780
cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct     840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg     900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaca gaagttgcag     960
ggccgcgtca caatgactac agacacttcc accagcacag cctacatgga actgagcagc    1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc    1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact    1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca    1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga gctgcagagc cagtcaaagt    1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat    1320
gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc    1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa    1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat    1500
caccatcatc attagagatc tgtcgac                                        1527
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<210> 180

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL2

<400> 180

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 181

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL3

<400> 181
gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780
cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaca gaagttgcag 960
ggccgcgtca caatgactac agacacttcc accagcacag cctacatgga actgagcagc 1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc 1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca 1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt 1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
caccatcatc attagagatc tgtcgac 1527

<210> 182

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL3

<400> 182

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg
405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 183

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL1

<400> 183

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gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc    60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac   120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct   180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat   240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg   300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc   360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct   420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg   480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga   540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa   600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat   660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg   720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg   780
cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct   840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg   900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaca gaagttgcag   960
ggccgcgtca caatgactac agacacttcc accagcacag cctacctgca aatgaacagc  1020
ctgaaaactg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc  1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact  1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttcagatgac ccagtctcca  1200
tctagcctgt ctgcatctgt cggggaccgt gtcaccatca cctgcagagc cagtcaaagt  1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat  1320
gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc  1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa  1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat  1500
caccatcatc attagagatc tgtcgac                                      1527
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<210> 184

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL1

<400> 184

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
            20   25   30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
        35   40   45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
    50   55   60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65   70   75   80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
                85   90   95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
            100   105   110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
        115   120   125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
    130   135   140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145   150   155   160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
                165   170   175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
            180   185   190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
        195   200   205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
    210   215   220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp

225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu
325 330 335

Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro
385 390 395 400

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 185

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL2

<400> 185

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caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct     180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat     240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg     300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc     360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct     420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg     480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga     540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa     600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat     660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg     720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg     780
cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct     840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg     900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaca gaagttgcag     960
ggccgcgtca caatgactac agacacttcc accagcacag cctacctgca aatgaacagc    1020
ctgaaaactg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc    1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact    1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca    1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga gctgcagagc cagtcaaagt    1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat    1320
gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc    1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa    1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat    1500
caccatcatc attagagatc tgtcgac                                        1527
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<210> 186

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL2

<400> 186

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu
325 330 335

Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu

485 490 495

Ile Lys

<210> 187

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL3

<400> 187

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180

gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240

cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300

acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360

tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420

gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480

aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540

gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600

tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660

ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720

ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780

cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840

ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900

gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaca gaagttgcag 960

ggccgcgtca caatgactac agacacttcc accagcacag cctacctgca aatgaacagc 1020

ctgaaaactg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc 1080

cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140

ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca 1200

gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt 1260

gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320

gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380

gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440

cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500

caccatcatc attagagatc tgtcgac 1527

<210> 188

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL3

<400> 188

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu
325 330 335

Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg
405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 189

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL1

<400> 189

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atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac     120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct     180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat     240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg     300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc     360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct     420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg     480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga     540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa     600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat     660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg     720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg     780
cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct     840
ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg     900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaga cagcgtcaag     960
ggccgcttca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc    1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc    1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact    1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttcagatgac ccagtctcca    1200
tctagcctgt ctgcatctgt cggggaccgt gtcaccatca cctgcagagc cagtcaaagt    1260
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gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320

gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380

gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440

cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500

caccatcatc attagagatc tgtcgac 1527

<210> 190

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL1

<400> 190

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
305 310 315 320

Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro
385 390 395 400

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
    450   455   460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465   470   475   480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
                485   490   495

Ile Lys

<210> 191

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL2

<400> 191
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atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180

gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240

cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300

acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360

tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420

gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480

aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540

gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600

tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660

ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720

ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780

cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840

ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900

gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaga cagcgtcaag 960

ggccgcttca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc 1020

ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc 1080

cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140

ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca 1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga gctgcagagc cagtcaaagt 1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
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caccatcatc attagagatc tgtcgac 1527

<210> 192

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL2

<400> 192

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met

134

145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
305 310 315 320

Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
        435   440   445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
    450   455   460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465   470   475   480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
                485   490   495

Ile Lys

<210> 193

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL3

<400> 193
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caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
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gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt 1260

gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320

gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380

gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440

cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500

caccatcatc attagagatc tgtcgac 1527

<210> 194

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL3

<400> 194

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
305 310 315 320

Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg

405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 195

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL1

<400> 195

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caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct     180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat     240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg     300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc     360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct     420
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aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga     540
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tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat     660
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ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg     780
cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct     840
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gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
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caccatcatc attagagatc tgtcgac 1527

<210> 196

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL1

<400> 196

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
305 310 315 320

Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro
385 390 395 400

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 197

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL2

<400> 197
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caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
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gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
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ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
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gaatggattg gatacattaa tcctagccgt ggttatacta attacaatca gaagttcaag 960
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gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
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caccatcatc attagagatc tgtcgac 1527

<210> 198

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL2

<400> 198

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
305 310 315 320

Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 199

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL3

<400> 199
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gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540

gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600

tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660

ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720

ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780

cagtcagggg ctgaagtgaa aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840

ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900

gaatggattg gatacattaa tcctagccgt ggttatacta attacaatca gaagttcaag 960

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gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt 1260

gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320

gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380

gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440

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caccatcatc attagagatc tgtcgac 1527

<210> 200

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL3

<400> 200

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His

146

65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
305 310 315 320

Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg
405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 201

<211> 45

<212> DNA

<213> artificial sequence

<220>

<223> standard linker

<400> 201
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttct 45

<210> 202

<211> 54

<212> DNA

<213> artificial sequence

<220>

<223> deimmunized linker

<400> 202
ggcgaaggta ctagtactgg ttctggtgga agtggaggtt caggtggagc agac 54

<210> 203

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3

<400> 203
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caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
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gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
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gcaatcatgt ctgcatctcc aggggagaag gtcaccatga cctgcagagc cagttcaagt 1260
gtaagttaca tgaactggta ccagcagaag tcaggcacct cccccaaaag atggatttat 1320
gacacatcca aagtggcttc tggagtccct tatcgcttca gtggcagtgg gtctgggacc 1380

tcatactctc tcacaatcag cagcatggag gctgaagatg ctgccactta ttactgccaa 1440

cagtggagta gtaacccgct cacgttcggt gctgggacca agctggagct gaaa 1494

<210> 204

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3

<400> 204

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser
260 265 270

Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
305 310 315 320

Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr Met
325 330 335

Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Leu Thr Val Ser Ser Val Glu Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Val Asp Asp Ile Gln Leu Thr Gln Ser Pro
385 390 395 400

Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg
405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser Gly
420 425 430

Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
450 455 460

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu
485 490 495

Leu Lys

<210> 205

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL1

<400> 205
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atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac 120

caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc 180

ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240

cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300

acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttctgg cggcggcggc 360

tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420

acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg 480

gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540

gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc 600

agcactgcct atttgcggat caacaacctc aaaaatgagg acatggctaa atacttctgt 660

gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720

accgtctcct ccggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780

aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840

tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt 900

aatcctagcc gtggttatac taattacgca gacagcgtca agggccgctt cacaatcact 960

acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact 1020

gcaacctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa 1080

ggcaccacgg tcaccgtctc ctcaggcgaa ggtactagta ctggttctgg tggaagtgga 1140

ggttcaggtg gagcagacga cattcagatg acccagtctc catctagcct gtctgcatct 1200

gtcggggacc gtgtcaccat cacctgcaga gccagtcaaa gtgtaagtta catgaactgg 1260

taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct 1320

tctggagtcc ctgctcgctt cagtggcagt gggtctggga ccgactactc tctcacaatc 1380

aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaacccg 1440

ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 206

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL1

<400> 206

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
            20   25   30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35   40   45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
    50   55   60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65   70   75   80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
                85   90   95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
            100   105   110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
        115   120   125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
    130   135   140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
145   150   155   160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
                165   170   175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
195 200 205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
210 215 220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
290 295 300

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
325 330 335

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
385 390 395 400

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu

450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 207

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL2

<400> 207
gacattatcc tgatccaatc tccaccttct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac 120

caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc 180

ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240

cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300

acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttctgg cggcggcggc 360

tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420

acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg 480

gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540

gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc 600

agcactgcct atttgcggat caacaacctc aaaaatgagg acatggctaa atacttctgt 660

gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720

accgtctcct ccggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780

aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840

tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt 900

aatcctagcc gtggttatac taattacgca gacagcgtca agggccgctt cacaatcact 960

acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact 1020

gcaacctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa 1080

ggcaccacgg tcaccgtctc ctcaggcgaa ggtactagta ctggttctgg tggaagtgga 1140

ggttcaggtg gagcagacga cattgtactg acccagtctc cagcaactct gtctctgtct 1200

ccaggggagc gtgccaccct gagctgcaga gccagtcaaa gtgtaagtta catgaactgg 1260

taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct 1320

tctggagtcc ctgctcgctt cagtggcagt gggtctggga ccgactactc tctcacaatc 1380

aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaacccg 1440

ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 208

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL2

<400> 208

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
            20   25   30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35   40   45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
    50   55   60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65   70   75   80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
                85   90   95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
            100   105   110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
        115   120   125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
    130   135   140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
145   150   155   160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
                165   170   175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe

180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
195 200 205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
210 215 220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
290 295 300

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
325 330 335

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
385 390 395 400

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 209

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL3

<400> 209

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atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac     120
caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc     180
ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat     240
cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg     300
acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttctgg cggcggcggc     360
tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag     420
acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg     480
gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga     540
gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc     600
agcactgcct atttgcggat caacaacctc aaaaatgagg acatggctaa atacttctgt     660
gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc     720
accgtctcct ccggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg     780
aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg     840
tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt     900
aatcctagcc gtggttatac taattacgca gacagcgtca agggccgctt cacaatcact     960
acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact    1020
gcaacctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa    1080
ggcaccacgg tcaccgtctc ctcaggcgaa ggtactagta ctggttctgg tggaagtgga    1140
ggttcaggtg gagcagacga cattgtactg acccagtctc cagcaactct gtctctgtct    1200
ccaggggagc gtgccaccct gacctgcaga gccagttcaa gtgtaagtta catgaactgg    1260
taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct    1320
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tctggagtcc ctgctcgctt cagtggcagt gggtctggga ccgactactc tctcacaatc 1380

aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaacccg 1440

ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 210

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL3

<400> 210

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
        195   200   205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
    210   215   220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
225   230   235   240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
                245   250   255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
            260   265   270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
        275   280   285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
    290   295   300

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
305   310   315   320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
                325   330   335

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
            340   345   350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        355   360   365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
    370   375   380

Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
385   390   395   400

Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser
                405   410   415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
            420   425   430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
        435   440   445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
    450   455   460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 211

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL1

<400> 211
gacattatcc tgatccaatc tccaccttct ttggctgtgt ctctagggca gagggccacc 60
atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac 120
caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc 180
ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240
cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300
acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420
acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg 480
gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540
gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc 600
agcactgcct atttgcggat caacaacctc aaaaatgagg acatggctaa atacttctgt 660
gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720
accgtctcct ccggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780
aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840
tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt 900
aatcctagcc gtggttatac taattacaat cagaagttca aggaccgcgt cacaatcact 960
acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact 1020
gcagtctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa 1080
ggcaccacgg tcaccgtctc ctcaggcgaa ggtactagta ctggttctgg tggaagtgga 1140
ggttcaggtg gagcagacga cattcagatg acccagtctc catctagcct gtctgcatct 1200
gtcggggacc gtgtcaccat cacctgcaga gccagtcaaa gtgtaagtta catgaactgg 1260
taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct 1320
tctggagtcc ctgctcgctt cagtggcagt gggtctggga ccgactactc tctcacaatc 1380

aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaacccg 1440

ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 212

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL1

<400> 212

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
195 200 205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
210 215 220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
290 295 300

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
325 330 335

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
385 390 395 400

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 213

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL2

<400> 213
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caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc 180
ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240
cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300
acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420
acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg 480
gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540
gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc 600
agcactgcct atttgcggat caacaacctc aaaaatgagg acatggctaa atacttctgt 660
gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720
accgtctcct ccggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780
aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840
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gcagtctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa 1080
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ccaggggagc gtgccaccct gagctgcaga gccagtcaaa gtgtaagtta catgaactgg 1260
taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct 1320
tctggagtcc ctgctcgctt cagtggcagt gggtctggga ccgactactc tctcacaatc 1380

aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaacccg 1440

ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 214

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL2

<400> 214

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
195 200 205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
210 215 220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
290 295 300

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
325 330 335

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
385 390 395 400

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro

465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 215

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL3

<400> 215

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caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc 180
ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240
cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300
acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420
acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg 480
gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540
gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc 600
agcactgcct atttgcggat caacaacctc aaaaatgagg acatggctaa atacttctgt 660
gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720
accgtctcct ccggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780
aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840
tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt 900
aatcctagcc gtggttatac taattacaat cagaagttca aggaccgcgt cacaatcact 960
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ccaggggagc gtgccaccct gacctgcaga gccagttcaa gtgtaagtta catgaactgg 1260
taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct 1320
tctggagtcc ctgctcgctt cagtggcagt gggtctggga ccgactactc tctcacaatc 1380
aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaacccg 1440

ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 216

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL3

<400> 216

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn

195 200 205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
210 215 220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
290 295 300

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
325 330 335

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
385 390 395 400

Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 217

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL1

<400> 217
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tcctccccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gacctcttac tctctcacaa tcagcagagt ggaggctgaa 240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
acaaaggtgg aaataaaagg tggtggtggt tctggcggcg gcggctccgg tggtggtggt 360
tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag 420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag 480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc 540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc 600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
cactacggta gtaactacgt agactacttt gactactggg gccaaggcac actagtcaca 720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaaa 780
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gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020
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accacggtca ccgtctcctc aggcgaaggt actagtactg gttctggtgg aagtggaggt 1140
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agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taacccgctc 1440

acgttcggtg gcgggaccaa ggtggagatc aaa 1473

<210> 218

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL1

<400> 218

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
385 390 395 400

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 219

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL2

<400> 219
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ttcagtggca gtgggtctgg gacctcttac tctctcacaa tcagcagagt ggaggctgaa 240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
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acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc 540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc 600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
cactacggta gtaactacgt agactacttt gactactggg gccaaggcac actagtcaca 720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaaa 780
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gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020
acctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc 1080
accacggtca ccgtctcctc aggcgaaggt actagtactg gttctggtgg aagtggaggt 1140
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agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taacccgctc 1440
acgttcggtg gcgggaccaa ggtggagatc aaa 1473

<210> 220

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL2

<400> 220

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
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Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
            20   25   30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
        35   40   45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100   105   110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
        115   120   125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
    130   135   140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
145   150   155   160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
                165   170   175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
            180   185   190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
        195   200   205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
385 390 395 400

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
175
485 490

<210> 221

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL3

<400> 221

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tcctccccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc     180
ttcagtggca gtgggtctgg gacctcttac tctctcacaa tcagcagagt ggaggctgaa     240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg     300
acaaaggtgg aaataaaagg tggtggtggt tctggcggcg gcggctccgg tggtggtggt     360
tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag     420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag     480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc     540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc     600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg     660
cactacggta gtaactacgt agactacttt gactactggg gccaaggcac actagtcaca     720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaaa     780
aaacctgggg cctcagtgaa ggtgtcctgc aaggcttctg gctacacctt tactaggtac     840
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gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca    1020
acctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc    1080
accacggtca ccgtctcctc aggcgaaggt actagtactg gttctggtgg aagtggaggt    1140
tcaggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca    1200
ggggagcgtg ccaccctgac ctgcagagcc agttcaagtg taagttacat gaactggtac    1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct    1320
ggagtccctg ctcgcttcag tggcagtggg tctgggaccg actactctct cacaatcaac    1380
agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taacccgctc    1440
acgttcggtg gcgggaccaa ggtggagatc aaa                                 1473
```

<210> 222

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL3

<400> 222

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1   5   10   15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
            20   25   30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
        35   40   45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100   105   110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
        115   120   125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
    130   135   140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
145   150   155   160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
                165   170   175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
            180   185   190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
        195   200   205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
385 390 395 400

Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys

485 490

<210> 223

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL1

<400> 223

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tcctccccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gacctcttac tctctcacaa tcagcagagt ggaggctgaa 240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
acaaaggtgg aaataaaagg tggtggtggt tctggcggcg gcggctccgg tggtggtggt 360
tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag 420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag 480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc 540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc 600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
cactacggta gtaactacgt agactacttt gactactggg gccaaggcac actagtcaca 720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaaa 780
aaacctgggg cctcagtgaa ggtgtcctgc aaggcttctg gctacacctt tactaggtac 840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat 900
cctagccgtg gttatactaa ttacaatcag aagttcaagg accgcgtcac aatcactaca 960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020
gtctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc 1080
accacggtca ccgtctcctc aggcgaaggt actagtactg gttctggtgg aagtggaggt 1140
tcaggtggag cagacgacat tcagatgacc cagtctccat ctagcctgtc tgcatctgtc 1200
ggggaccgtg tcaccatcac ctgcagagcc agtcaaagtg taagttacat gaactggtac 1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct 1320
ggagtccctg ctcgcttcag tggcagtggg tctgggaccg actactctct cacaatcaac 1380
agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taacccgctc 1440
acgttcggtg gcgggaccaa ggtggagatc aaa 1473

<210> 224

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL1

<400> 224

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser

180

210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
385 390 395 400

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 225

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL2

<400> 225
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tcctccccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gacctcttac tctctcacaa tcagcagagt ggaggctgaa 240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
acaaaggtgg aaataaaagg tggtggtggt tctggcggcg gcggctccgg tggtggtggt 360
tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag 420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag 480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc 540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc 600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
cactacggta gtaactacgt agactacttt gactactggg gccaaggcac actagtcaca 720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaaa 780
aaacctgggg cctcagtgaa ggtgtcctgc aaggcttctg gctacacctt tactaggtac 840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat 900
cctagccgtg gttatactaa ttacaatcag aagttcaagg accgcgtcac aatcactaca 960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020
gtctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc 1080
accacggtca ccgtctcctc aggcgaaggt actagtactg gttctggtgg aagtggaggt 1140
tcaggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca 1200
ggggagcgtg ccaccctgag ctgcagagcc agtcaaagtg taagttacat gaactggtac 1260
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agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taacccgctc 1440
acgttcggtg gcgggaccaa ggtggagatc aaa 1473

<210> 226

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL2

<400> 226

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1   5   10   15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
            20   25   30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
        35   40   45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
            100   105   110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
        115   120   125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
    130   135   140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
145   150   155   160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
                165   170   175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
            180   185   190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
        195   200   205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
    210   215   220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
385 390 395 400

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 227

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL3

<400> 227
caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca 60
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tcctccccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gacctcttac tctctcacaa tcagcagagt ggaggctgaa 240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
acaaaggtgg aaataaaagg tggtggtggt tctggcggcg gcggctccgg tggtggtggt 360
tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag 420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag 480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc 540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc 600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
cactacggta gtaactacgt agactacttt gactactggg gccaaggcac actagtcaca 720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaaa 780
aaacctgggg cctcagtgaa ggtgtcctgc aaggcttctg gctacacctt tactaggtac 840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat 900
cctagccgtg gttatactaa ttacaatcag aagttcaagg accgcgtcac aatcactaca 960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020
gtctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc 1080
accacggtca ccgtctcctc aggcgaaggt actagtactg gttctggtgg aagtggaggt 1140
tcaggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca 1200
ggggagcgtg ccaccctgac ctgcagagcc agttcaagtg taagttacat gaactggtac 1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct 1320
ggagtccctg ctcgcttcag tggcagtggg tctgggaccg actactctct cacaatcaac 1380
agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taacccgctc 1440
acgttcggtg gcgggaccaa ggtggagatc aaa 1473

<210> 228

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL3

<400> 228

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
385 390 395 400

Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 229

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 1

<400> 229

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1   5   10   15

Ser Val Lys Met Ser Cys Lys Thr Ser
            20   25

<210> 230

<211> 15

<212> PRT

<213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 2

<400> 230

Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
1   5   10   15

<210> 231

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 3

<400> 231

Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln
1   5   10   15

Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg
            20   25   30

<210> 232

<211> 11

<212> PRT

<213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 4

<400> 232

Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
1   5   10

<210> 233

<211> 6

<212> PRT

<213> artificial sequence

<220>

<223> Sequence motif

<400> 233

Ala Ser Gly Tyr Thr Phe
1   5

<210> 234

<211> 4

<212> PRT

<213> artificial sequence

<220>

<223> Sequence motif

<400> 234

Met Glu Leu Ser
1

<210> 235

<211> 5

<212> PRT

<213> artificial sequence

<220>

<223> Sequence motif

<400> 235

Ile Thr Thr Asp Lys
1 5

<210> 236

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVH5VL1 LHHL

<400> 236
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atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120

tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360

ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420

gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540

ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600

gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660

gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720

gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca 780

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tctgaggaca ctgcaaccta ttactgtgca agatattatg atgatcatta ctgccttgac 1080

tactggggcc aaggcaccac ggtcaccgtc tcctcaggcg aaggtactag tactggttct 1140

ggtggaagtg gaggttcagg tggagcagac gacattcaga tgacccagtc tccatctagc 1200

ctgtctgcat ctgtcgggga ccgtgtcacc atcacctgca gagccagtca aagtgtaagt 1260

tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320

190

tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380

tctctcacaa tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440

agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 237

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVH5VL1 LHHL

<400> 237

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1   5   10   15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20   25   30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
                85   90   95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
            100   105   110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser
        115   120   125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
    130   135   140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145   150   155   160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
                165   170   175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
            180   185   190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg
305 310 315 320

Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
325 330 335

Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr
340 345 350

Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
385 390 395 400

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
405 410 415

Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490 495

<210> 238

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVH5VL1 HLHL

<400> 238
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atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc 840
tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggtctggaa 900
tggattggat acattaatcc tagccgtggt tatactaatt acgcagacag cgtcaagggc 960
cgcttcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020
cgttctgagg acactgcaac ctattactgt gcaagatatt atgatgatca ttactgcctt 1080
gactactggg gccaaggcac cacggtcacc gtctcctcag gcgaaggtac tagtactggt 1140
tctggtggaa gtggaggttc aggtggagca gacgacattc agatgaccca gtctccatct 1200
agcctgtctg catctgtcgg ggaccgtgtc accatcacct gcagagccag tcaaagtgta 1260
agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac 1320
acatccaaag tggcttctgg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac 1380

tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440

tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a 1491

<210> 239

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVH5VL1 HLHL

<400> 239

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly
305 310 315 320

Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser
385 390 395 400

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

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                                                195
Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
465                 470                 475                 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
                485                 490                 495

Lys
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<210> 240

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVL1VH5 LHLH

<400> 240

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atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc     120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg     180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc     240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat     300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc     360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg     420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac     480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt     540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact     600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct     660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa     720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattcagat gacccagtct     780
ccatctagcc tgtctgcatc tgtcggggac cgtgtcacca tcacctgcag agccagtcaa     840
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt     900
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg     960
accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc    1020
caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaaggc    1080
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacgtccaa    1140
ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag    1200
gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag    1260
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ggtctggaat ggattggata cattaatcct agccgtggtt atactaatta cgcagacagc 1320

gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1380

agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1440

tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 241

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVL1VH5 LHLH

<400> 241

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

197
Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
245 250 255

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
260 265 270

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
420 425 430

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg

450 455 460

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
485 490 495

<210> 242

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVL1VH5 HLLH

<400> 242
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattca gatgacccag 780
tctccatcta gcctgtctgc atctgtcggg gaccgtgtca ccatcacctg cagagccagt 840
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 900
atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 960
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1080
ggcgaaggta ctagtactgg ttctggtgga agtggaggtt caggtggagc agacgacgtc 1140
caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtgaa ggtgtcctgc 1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260
cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacgcagac 1320

agcgtcaagg gccgcttcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380

ctgagcagcc tgcgttctga ggacactgca acctattact gtgcaagata ttatgatgat 1440

cattactgcc ttgactactg ggccaaggc accacggtca ccgtctcctc a 1491

<210> 243

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVL1VH5 HLLH

<400> 243

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala

200
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
245 250 255

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
260 265 270

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
420 425 430

Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
450 455 460

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

Ser

<210> 244

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVH5VL2 HLHL

<400> 244
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc 840
tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggtctggaa 900
tggattggat acattaatcc tagccgtggt tatactaatt acgcagacag cgtcaagggc 960
cgcttcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020
cgttctgagg acactgcaac ctattactgt gcaagatatt atgatgatca ttactgcctt 1080
gactactggg gccaaggcac cacggtcacc gtctcctcag gcgaaggtac tagtactggt 1140
tctggtggaa gtggaggttc aggtggagca gacgacattg tactgaccca gtctccagca 1200

actctgtctc tgtctccagg ggagcgtgcc accctgagct gcagagccag tcaaagtgta 1260
agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac 1320
acatccaaag tggcttctgg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac 1380
tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440
tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a 1491

<210> 245

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVH5VL2 HLHL

<400> 245

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly
305 310 315 320

Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
385 390 395 400

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
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Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
485 490 495

Lys

<210> 246

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVL2VH5 LHLH

<400> 246

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gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
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ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
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gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260

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gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1380

agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1440

tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 247

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVL2VH5 LHLH

<400> 247

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1   5   10   15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
            20   25   30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
                85   90   95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
            100   105   110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115   120   125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
    130   135   140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145   150   155   160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
260 265 270

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
420 425 430

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
450 455 460

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
485 490 495

<210> 248

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVL2VH5 HLLH

<400> 248
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aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
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cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgacccag 780
tctccagcaa ctctgtctct gtctccaggg gagcgtgcca ccctgagctg cagagccagt 840
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 900
atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 960
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caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtgaa ggtgtcctgc 1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260
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agcgtcaagg gccgcttcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380
ctgagcagcc tgcgttctga ggacactgca acctattact gtgcaagata ttatgatgat 1440
cattactgcc ttgactactg gggccaaggc accacggtca ccgtctcctc a 1491

<210> 249

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVL2VH5 HLLH

<400> 249

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1   5   10   15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
            20   25   30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
        35   40   45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
    50   55   60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65   70   75   80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
                85   90   95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
            100   105   110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115   120   125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
    130   135   140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145   150   155   160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
245 250 255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
260 265 270

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
420 425 430

Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile

435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
450 455 460

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

Ser

<210> 250

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10 VH5VL3 LHHL

<400> 250
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tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360

ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420

gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540

ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600

gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660

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ctgtctctgt ctccagggga gcgtgccacc ctgacctgca gagccagttc aagtgtaagt 1260

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tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380

tctctcacaa tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440

agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 251

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VH5VL3 LHHL

<400> 251

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn

212

145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg
305 310 315 320

Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
325 330 335

Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr
340 345 350

Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr
385 390 395 400

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser
405 410 415

Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490 495

<210> 252

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VH5VL3 HLHL

<400> 252
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aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
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<210> 253

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VH5VL3 HLHL

<400> 253

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly
305 310 315 320

Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
385 390 395 400

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala
405 410 415

Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
485 490 495

Lys

<210> 254

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VL3VH5 LHLH

<400> 254
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tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360

ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420

gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540

ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600

gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660

gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720

gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gacccagtct 780

ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca 840

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tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960

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gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1440
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 255

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VL3VH5 LHLH

<400> 255

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
260 265 270

Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
420 425 430

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
450 455 460

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
485 490 495

<210> 256

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VL3VH5 HLLH

<400> 256
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aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
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cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
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ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgacccag 780
tctccagcaa ctctgtctct gtctccaggg gagcgtgcca ccctgacctg cagagccagt 840
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gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020

tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1080

ggcgaaggta ctagtactgg ttctggtgga agtggaggtt caggtggagc agacgacgtc 1140

caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtgaa ggtgtcctgc 1200

aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260

cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacgcagac 1320

agcgtcaagg gccgcttcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380

ctgagcagcc tgcgttctga ggacactgca acctattact gtgcaagata ttatgatgat 1440

cattactgcc ttgactactg gggccaaggc accacggtca ccgtctcctc a 1491

<210> 257

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VL3VH5 HLLH

<400> 257

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145   150   155   160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
                165   170   175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
            180   185   190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
        195   200   205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
    210   215   220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225   230   235   240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
                245   250   255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
            260   265   270

Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp
        275   280   285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
    290   295   300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
305   310   315   320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
                325   330   335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
            340   345   350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
        355   360   365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
    370   375   380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
385   390   395   400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
                405   410   415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser

420 425 430

Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
450 455 460

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

Ser

<210> 258

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VH7VL1 LHHL

<400> 258

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tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg     180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc     240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat     300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc     360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg     420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac     480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt     540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact     600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct     660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa     720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca     780
ggggctgaag tgaaaaaacc tggggcctca gtgaaggtgt cctgcaaggc ttctggctac     840
acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg     900
attggataca ttaatcctag ccgtggttat actaattaca atcagaagtt caaggaccgc     960
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gtcacaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt 1020

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tactggggcc aaggcaccac ggtcaccgtc tcctcaggcg aaggtactag tactggttct 1140

ggtggaagtg gaggttcagg tggagcagac gacattcaga tgacccagtc tccatctagc 1200

ctgtctgcat ctgtcgggga ccgtgtcacc atcacctgca gagccagtca aagtgtaagt 1260

tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320

tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380

tctctcacaa tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440

agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 259

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VH7VL1 LHHL

<400> 259

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly

130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg
305 310 315 320

Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
325 330 335

Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr
340 345 350

Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
385 390 395 400

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
405 410 415

Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490 495

<210> 260

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VH7VL1 HLHL

<400> 260
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tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
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aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
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cgcgtcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020

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tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440

tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a 1491

<210> 261

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VH7VL1 HLHL

<400> 261

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp
305 310 315 320

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser
385 390 395 400

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
485 490 495

Lys

<210> 262

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VL1VH7 LHLH

<400> 262
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tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360

ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420

gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540

ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600

gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660

gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720

gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattcagat gacccagtct 780

ccatctagcc tgtctgcatc tgtcggggac cgtgtcacca tcacctgcag agccagtcaa 840

agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900

tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960

accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1020

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agcagcctgc gttctgagga cactgcagtc tattactgtg caagatatta tgatgatcat 1440

tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 263

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VL1VH7 LHLH

<400> 263

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
245 250 255

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
260 265 270

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
420 425 430

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
450 455 460

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
485 490 495

<210> 264

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VL1VH7 HLLH

<400> 264
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattca gatgacccag 780
tctccatcta gcctgtctgc atctgtcggg gaccgtgtca ccatcacctg cagagccagt 840
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 900

atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 960
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1080
ggcgaaggta ctagtactgg ttctggtgga agtggaggtt caggtggagc agacgacgtc 1140
caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtgaa ggtgtcctgc 1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260
cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacaatcag 1320
aagttcaagg accgcgtcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380
ctgagcagcc tgcgttctga ggacactgca gtctattact gtgcaagata ttatgatgat 1440
cattactgcc ttgactactg gggccaaggc accacggtca ccgtctcctc a 1491

<210> 265

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VL1VH7 HLLH

<400> 265

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1   5   10   15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
            20   25   30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
        35   40   45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
    50   55   60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65   70   75   80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
                85   90   95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
            100   105   110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115   120   125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
245 250 255

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
260 265 270

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg

405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
420 425 430

Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile
435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
450 455 460

Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

Ser

<210> 266

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VH7VL2 LHHL

<400> 266

gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60

atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120

tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360

ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420

gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540

ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600

gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660

gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720

gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca 780

ggggctgaag tgaaaaaacc tggggcctca gtgaaggtgt cctgcaaggc ttctggctac 840

acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg 900
attggataca ttaatcctag ccgtggttat actaattaca atcagaagtt caaggaccgc 960
gtcacaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt 1020
tctgaggaca ctgcagtcta ttactgtgca agatattatg atgatcatta ctgccttgac 1080
tactggggcc aaggcaccac ggtcaccgtc tcctcaggcg aaggtactag tactggttct 1140
ggtggaagtg gaggttcagg tggagcagac gacattgtac tgacccagtc tccagcaact 1200
ctgtctctgt ctccagggga gcgtgccacc ctgagctgca gagccagtca aagtgtaagt 1260
tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320
tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380
tctctcacaa tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440
agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 267

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VH7VL2 LHHL

<400> 267

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg
305 310 315 320

Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
325 330 335

Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr
340 345 350

Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr
385 390 395 400

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
405 410 415

Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490 495

<210> 268

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VH7VL2 HLHL

<400> 268
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60

atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120

aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180

tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240

tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300

aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360

ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420

cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480

agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540

ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600

gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660

gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720

gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780

tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc 840

tacacccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggtctggaa 900

tggattggat acattaatcc tagccgtggt tatactaatt acaatcagaa gttcaaggac 960

cgcgtcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020

cgttctgagg acactgcagt ctattactgt gcaagatatt atgatgatca ttactgcctt 1080

gactactggg gccaaggcac cacggtcacc gtctcctcag gcgaaggtac tagtactggt 1140

tctggtggaa gtggaggttc aggtggagca gacgacattg tactgaccca gtctccagca 1200

actctgtctc tgtctccagg ggagcgtgcc accctgagct gcagagccag tcaaagtgta 1260

agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac 1320

acatccaaag tggcttctgg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac 1380

tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440

tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a 1491

<210> 269

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VH7VL2 HLHL

<400> 269

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp
305 310 315 320

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
385 390 395 400

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
485 490 495

Lys

<210> 270

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VL2VH7 LHLH

<400> 270

gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60

atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120

tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360

ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420

gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540

ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600

gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660

gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720

gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gacccagtct 780

ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa 840
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960
accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1020
caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaaggc 1080
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacgtccaa 1140
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gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
ggtctggaat ggattggata cattaatcct agccgtggtt atactaatta caatcagaag 1320
ttcaaggacc gcgtcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
agcagcctgc gttctgagga cactgcagtc tattactgtg caagatatta tgatgatcat 1440
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 271

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VL2VH7 LHLH

<400> 271

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
260 265 270

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
420 425 430

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
450 455 460

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
485 490 495

<210> 272

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VL2VH7 HLLH

<400> 272

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60

atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120

aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180

tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240

tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300

aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360

ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420

cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480

agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540

ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600

gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660

gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720

gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgacccag 780

tctccagcaa ctctgtctct gtctccaggg gagcgtgcca ccctgagctg cagagccagt 840
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aagttcaagg accgcgtcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380
ctgagcagcc tgcgttctga ggacactgca gtctattact gtgcaagata ttatgatgat 1440
cattactgcc ttgactactg gggccaaggc accacggtca ccgtctcctc a 1491

<210> 273

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VL2VH7 HLLH

<400> 273

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
245 250 255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
260 265 270

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys

385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
420 425 430

Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile
435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
450 455 460

Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

Ser

<210> 274

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VH7VL3 LHHL

<400> 274
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tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360

ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420

gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540

ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600

gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660

gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720

gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca 780
ggggctgaag tgaaaaaacc tggggcctca gtgaaggtgt cctgcaaggc ttctggctac 840
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attggataca ttaatcctag ccgtggttat actaattaca atcagaagtt caaggaccgc 960
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tactggggcc aaggcaccac ggtcaccgtc tcctcaggcg aaggtactag tactggttct 1140
ggtggaagtg gaggttcagg tggagcagac gacattgtac tgacccagtc tccagcaact 1200
ctgtctctgt ctccagggga gcgtgccacc ctgacctgca gagccagttc aagtgtaagt 1260
tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320
tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380
tctctcacaa tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440
agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 275

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VH7VL3 LHHL

<400> 275

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile

100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg
305 310 315 320

Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
325 330 335

Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr
340 345 350

Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr
385 390 395 400

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser
405 410 415

Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490 495

<210> 276

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VH7VL3 HLHL

<400> 276
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atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720

gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780

tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc 840

tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggtctggaa 900

tggattggat acattaatcc tagccgtggt tatactaatt acaatcagaa gttcaaggac 960

cgcgtcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020

cgttctgagg acactgcagt ctattactgt gcaagatatt atgatgatca ttactgcctt 1080

gactactggg gccaaggcac cacggtcacc gtctcctcag gcgaaggtac tagtactggt 1140

tctggtggaa gtggaggttc aggtggagca gacgacattg tactgaccca gtctccagca 1200

actctgtctc tgtctccagg ggagcgtgcc accctgacct gcagagccag ttcaagtgta 1260

agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac 1320

acatccaaag tggcttctgg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac 1380

tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440

tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a 1491

<210> 277

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VH7VL3 HLHL

<400> 277

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115   120   125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
    130   135   140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145   150   155   160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
                165   170   175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
            180   185   190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
        195   200   205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
    210   215   220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225   230   235   240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
                245   250   255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
            260   265   270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
        275   280   285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
    290   295   300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp
305   310   315   320

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
                325   330   335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            340   345   350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
        355   360   365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
    370   375   380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
385 390 395 400

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala
405 410 415

Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
485 490 495

Lys

<210> 278

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VL3VH7 LHLH

<400> 278
gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60

atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120

tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180

gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300

ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360

ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420

gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540

ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600

gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660

gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gacccagtct 780
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca 840
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960
accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1020
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gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacgtccaa 1140
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gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
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ttcaaggacc gcgtcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
agcagcctgc gttctgagga cactgcagtc tattactgtg caagatatta tgatgatcat 1440
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 279

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VL3VH7 LHLH

<400> 279

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
260 265 270

Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
355 360 365

255
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
420 425 430

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
450 455 460

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
485 490 495

<210> 280

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VL3VH7 HLLH

<400> 280
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
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aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660

gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720

gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgacccag 780

tctccagcaa ctctgtctct gtctccaggg gagcgtgcca ccctgacctg cagagccagt 840

tcaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 900

atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 960

gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020

tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1080

ggcgaaggta ctagtactgg ttctggtgga agtggaggtt caggtggagc agacgacgtc 1140

caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtgaa ggtgtcctgc 1200

aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260

cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacaatcag 1320

aagttcaagg accgcgtcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380

ctgagcagcc tgcgttctga ggacactgca gtctattact gtgcaagata ttatgatgat 1440

cattactgcc ttgactactg gggccaaggc accacggtca ccgtctcctc a 1491

<210> 281

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VL3VH7 HLLH

<400> 281

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

257

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
245 250 255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
260 265 270

Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp
275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln

370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
420 425 430

Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile
435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
450 455 460

Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

Ser

<210> 282

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL1/VH5x4-7 LHHL

<400> 282

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atcacctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120

aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480

gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540

tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660

gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720

gtctcctccg gaggtggtgg atccgaggtg cagctgctcg agcagtctgg agctgagctg 780

gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaaac 840

tatggtttaa gctgggtgaa gcagaggcct ggacaggtcc ttgagtggat tggagaggtt 900

tatcctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 960

gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct 1020

gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat 1080

gtctggggcc aagggaccac ggtcaccgtc tcctcaggtg gtggtggttc tggcggcggc 1140

ggctccggtg gtggtggttc tgagctcgtg atgacccaga ctccactctc cctgcctgtc 1200

agtcttggag atcaagcctc catctcttgc agatctagtc agagccttgt acacagtaat 1260

ggaaacacct atttacattg gtacctgcag aagccaggcc agtctccaaa gctcctgatc 1320

tacaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg 1380

acagatttca cactcaagat cagcagagtg gaggctgagg atctgggagt ttatttctgc 1440

tctcaaagta cacatgttcc gtacacgttc ggaggggga ccaagcttga gatcaaa 1497

<210> 283

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1/VH5x4-7 LHHL

<400> 283

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr

260

85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 284

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL1x4-7 HLHL

<400> 284
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480

agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600

agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660

acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720

gagatcaaat ccggaggtgg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780

ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca 840

aactatggtt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag 900

gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960

actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac 1020

tctgcggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctggtacttc 1080

gatgtctggg gccaagggac cacggtcacc gtctcctcag gtggtggtgg ttctggcggc 1140

ggcggctccg gtggtggtgg ttctgagctc gtgatgaccc agactccact ctccctgcct 1200

gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260

aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 1320

atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 1380

gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440

tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500

<210> 285

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL1x4-7 HLHL

<400> 285

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 286

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL1/VH5x4-7 LHLH

<400> 286
gacattcaga tgacccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc 60

atcacctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120

aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720
gtctcctccg gaggtggtgg atccgagctc gtgatgaccc agactccact ctccctgcct 780
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aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 900
atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 960
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1020
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aagggcaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc 1380
agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440
aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctcctca 1497

<210> 287

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1/VH5x4-7 LHLH

<400> 287

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
325 330 335

267
Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 288

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL1x4-7 HLLH

<400> 288
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgag ctcgtgatga cccagactcc actctccctg 780
cctgtcagtc ttggagatca agcctccatc tcttgcagat ctagtcagag ccttgtacac 840
agtaatggaa acacctattt acattggtac ctgcagaagc caggccagtc tccaaagctc 900
ctgatctaca aagtttccaa ccgattttct ggggtcccag acaggttcag tggcagtgga 960
tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat 1020
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aaaggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctga ggtgcagctg 1140
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gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
gtccttgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag 1320
ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440
actaactacg actggtactt cgatgtctgg ggccaaggga ccacggtcac cgtctcctca 1500

<210> 289

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL1x4-7 HLLH

<400> 289

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp

270

325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
485 490 495

Thr Val Ser Ser
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<210> 290

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL2/VH5x4-7 LHHL

<400> 290

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ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

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<210> 291

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL2/VH5x4-7 LHHL

<400> 291

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
            20   25   30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr

35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 292

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL2/VH5x4-7 LHLH

<400> 292
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480

gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540

tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660

gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720

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gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 840

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atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 960

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aagggcaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc 1380

agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440

aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctcctca 1497

<210> 293

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL2/VH5x4-7 LHLH

<400> 293

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
            20   25   30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 294

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH5x4-7 LHHL

<400> 294
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480

gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540

tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660

gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720

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<210> 295

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL3/VH5x4-7 LHHL

<400> 295

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
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Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
275 280 285

279
Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 296

<211> 1503

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL3x4-7 HLHL

<400> 296
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<210> 297

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL3x4-7 HLHL

<400> 297

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 298

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH5x4-7 LHLH

<400> 298
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
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agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440
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<210> 299

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL3/VH5x4-7 LHLH

<400> 299

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
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Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
245 250 255

285
Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 300

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL3x4-7 HLLH

<400> 300
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
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agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgag ctcgtgatga cccagactcc actctccctg 780
cctgtcagtc ttggagatca agcctccatc tcttgcagat ctagtcagag ccttgtacac 840
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ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440
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<210> 301

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL3x4-7 HLLH

<400> 301

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
                85   90   95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
        115   120   125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
    130   135   140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145   150   155   160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
                165   170   175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
            180   185   190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
        195   200   205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
    210   215   220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225   230   235   240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr

288

245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
485 490 495

Thr Val Ser Ser
500

<210> 302

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH7x4-7 LHHL

<400> 302
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720
gtctcctccg gaggtggtgg atccgaggtg cagctgctcg agcagtctgg agctgagctg 780
gcgaggcctg ggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaaac 840
tatggtttaa gctgggtgaa gcagaggcct ggacaggtcc ttgagtggat tggagaggtt 900
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acagatttca cactcaagat cagcagagtg gaggctgagg atctgggagt ttatttctgc 1440
tctcaaagta cacatgttcc gtacacgttc ggaggggga ccaagcttga gatcaaa 1497

<210> 303

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH7x4-7 LHHL

<400> 303

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 304

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7-VL1x4-7 HLHL

<400> 304
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
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acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
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gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440
tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500

<210> 305

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7-VL1x4-7 HLHL

<400> 305

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 306

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL1-VH7x4-7 LHLH

<400> 306
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atcacctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120

aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480

gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540

tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660

gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720

gtctcctccg gaggtggtgg atccgagctc gtgatgaccc agactccact ctccctgcct 780

gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 840

aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 900

atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 960

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tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1080

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cttgagtgga ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagttc 1320

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agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440

aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctcctca 1497

<210> 307

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1-VH7x4-7 LHLH

<400> 307

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

297
Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr

485 490 495

Val Ser Ser

<210> 308

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7-VL1x4-7 HLLH

<400> 308

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actaactacg actggtactt cgatgtctgg ggccaaggga ccacggtcac cgtctcctca 1500

<210> 309

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7-VL1x4-7 HLLH

<400> 309

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser

300

195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
485 490 495

Thr Val Ser Ser
500

<210> 310

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL2VH7x4-7 LHHL

<400> 310
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
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gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660
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tacaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg 1380

acagatttca cactcaagat cagcagagtg gaggctgagg atctgggagt ttatttctgc 1440

tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa 1497

<210> 311

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL2VH7x4-7 LHHL

<400> 311

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 312

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL2x4-7 HLHL

<400> 312
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gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
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gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440

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<210> 313

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL2x4-7 HLHL

<400> 313

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

307

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 314

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL2VH7x4-7 LHLH

<400> 314
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
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cttgagtgga ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagttc 1320

aagggcaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc 1380

agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440

aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctcctca 1497

<210> 315

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL2VH7x4-7 LHLH

<400> 315

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

309
Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala

435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 316

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL2x4-7 HLLH

<400> 316

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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360

gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420

ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480

agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600

agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660

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<210> 317

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL2x4-7 HLLH

<400> 317

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys

312

145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
485 490 495

Thr Val Ser Ser
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<210> 318

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH7x4-7 LHHL

<400> 318

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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480

gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540

tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660

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tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa 1497

<210> 319

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH7x4-7 LHHL

<400> 319

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
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Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
            20   25   30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
        35   40   45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
            100   105   110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
        115   120   125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
    130   135   140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
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Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 320

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL3x4-7 HLHL

<400> 320
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<210> 321
<211> 500
<212> PRT
<213> artificial sequence

<220>
<223> VH7VL3x4-7 HLHL
<400> 321

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

319

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
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<210> 322

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH7x4-7 LHLH

<400> 322
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accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
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<210> 323

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH7x4-7 LHLH

<400> 323

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
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Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
            20   25   30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
        35   40   45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
            100   105   110

321

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala

322

385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 324

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL3x4-7 HLLH

<400> 324

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<210> 325

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL3x4-7 HLLH

<400> 325

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly

100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
485 490 495

Thr Val Ser Ser
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<210> 326

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHHL

<400> 326
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480

gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540

tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660
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gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcactgtcag 1440
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<210> 327

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHHL

<400> 327

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 328

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL1xCD19 HLHL

<400> 328

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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac     180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac     240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat     300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc     360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag     420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc     480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc     540
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acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
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tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
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ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
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acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 329

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL1xCD19 HLHL

<400> 329

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
340 345 350

331

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 330

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHLH

<400> 330
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accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600
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gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
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<210> 331

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHLH

<400> 331

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

333
Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly

334

340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 332

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL1xCD19 HLLH

<400> 332
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360

gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420
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<210> 333

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL1xCD19 HLLH

<400> 333

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val

336

50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
245 250 255

Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
260 265 270

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 334

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL2/VH5xCD19 LHHL

<400> 334

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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
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agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660
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gatgcatcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctgggaca 1380
gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcactgtcag 1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa 1494

<210> 335

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL2/VH5xCD19 LHHL

<400> 335

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
305 310 315 320

340

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 336

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL2xCD19 HLHL

<400> 336

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780
gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
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tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
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gactactggg gccaagggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140
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tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 1380
acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 337

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL2xCD19 HLHL

<400> 337

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
290 295 300

343
Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 338

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL2/VH5xCD19

<400> 338
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ctgagctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660
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gtctcctccg gaggtggtgg atccgatatc cagctgaccc agtctccagc ttctttggct 780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840
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tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggtcttgag 1260
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gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

<210> 339

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL2/VH5xCD19

<400> 339

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser

346

290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 340

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL2xCD19 HLLH

<400> 340
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
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ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctcctcc 1497

<210> 341

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL2xCD19 HLLH

<400> 341

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
245 250 255

Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
260 265 270

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 342

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH5xCD19 LHHL

<400> 342
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
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agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660
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gtctcctccg gaggtggtgg atcccaggtg cagctgcagc agtctggggc tgagctggtg 780
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cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca 960
gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg 1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac 1080
tactggggcc aagggaccac ggtcaccgtc tcctccggtg gtggtggttc tggcggcggc 1140
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gatagttatt tgaactggta ccaacagatt ccaggacagc cacccaaact cctcatctat 1320
gatgcatcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctgggaca 1380
gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcactgtcag 1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa 1494

<210> 343

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH5xCD19 LHHL

<400> 343

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 344

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL3xCD19 HLHL

<400> 344
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780
gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
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tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
gactactggg gccaagggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140
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gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 1380
acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 345

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL3xCD19 HLHL

<400> 345

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
245 250 255

355

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 346

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH5xCD19 LHLH

<400> 346
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720
gtctcctccg gaggtggtgg atccgatatc cagctgaccc agtctccagc ttctttggct 780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900
tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 960
acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1020
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt 1080
ggtggtggtt ctggcggcgg cggctccggt ggtggtggtt ctcaggtgca gctgcagcag 1140
tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggtcttgag 1260
tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaagggt 1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380
gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

<210> 347

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH5xCD19 LHLH

<400> 347

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro

358

245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 348

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL3xCD19 HLLH

<400> 348

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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac     180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac     240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat     300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc     360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta     420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc     480
agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc     540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc     600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc     660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg     720
gagatcaaat ccggaggtgg tggatccgat atccagctga cccagtctcc agcttctttg     780
gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat     840
gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactcctc     900
atctatgatg catccaatct agtttctggg atcccaccca ggtttagtgg cagtgggtct     960
gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac    1020
tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa    1080
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ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt    1260
gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag    1320
ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc    1380
ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc    1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctcctcc       1497
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<210> 349

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL3xCD19 HLLH

<400> 349

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
                85   90   95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
        115   120   125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
    130   135   140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145   150   155   160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
                165   170   175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
            180   185   190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
        195   200   205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
    210   215   220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225   230   235   240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
245 250 255

Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
260 265 270

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 350

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH7xCD19 LHHL

<400> 350

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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc     180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa     240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg     300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca     360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc     420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg     480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt     540
tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc     600
agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt     660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc     720
gtctcctccg gaggtggtgg atcccaggtg cagctgcagc agtctggggc tgagctggtg     780
aggcctgggt cctcagtgaa gatttcctgc aaggcttctg gctatgcatt cagtagctac     840
tggatgaact gggtgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg     900
cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca     960
gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg    1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac    1080
tactggggcc aagggaccac ggtcaccgtc tcctccggtg gtggtggttc tggcggcggc    1140
ggctccggtg gtggtggttc tgatatccag ctgacccagt ctccagcttc tttggctgtg    1200
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gatagttatt tgaactggta ccaacagatt ccaggacagc cacccaaact cctcatctat    1320
gatgcatcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctgggaca    1380
gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcactgtcag    1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa           1494
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<210> 351

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH7xCD19 LHHL

<400> 351

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
            20   25   30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
        35   40   45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
            100   105   110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
        115   120   125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
    130   135   140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145   150   155   160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
                165   170   175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
            180   185   190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
        195   200   205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
    210   215   220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 352

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL1xCD19 HLHL

<400> 352

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780
gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt 900
tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
gactactggg gccaagggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140
ggcggctccg gtggtggtgg ttctgatatc cagctgaccc agtctccagc ttctttggct 1200
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 1380
acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 353

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL1xCD19 HLHL

<400> 353

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu

485 490 495

Glu Ile Lys

<210> 354

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH7xCD19 LHLH

<400> 354

gacattcaga tgacccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc 60
atcacctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720
gtctcctccg gaggtggtgg atccgatatc cagctgaccc agtctccagc ttctttggct 780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900
tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 960
acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1020
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt 1080
ggtggtggtt ctggcggcgg cggctccggt ggtggtggtt ctcaggtgca gctgcagcag 1140
tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggtcttgag 1260
tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaagggt 1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380
gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440

tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

<210> 355

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH7xCD19 LHLH

<400> 355

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser

370

195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 356

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL1xCD19 HLLH

<400> 356
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgat atccagctga cccagtctcc agcttctttg 780
gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat 840
gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactcctc 900
atctatgatg catccaatct agtttctggg atcccaccca ggtttagtgg cagtgggtct 960
gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac 1020
tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa 1080
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag 1140
cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttcctg caaggcttct 1200
ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt 1260
gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag 1320

ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc 1380

ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440

cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctcctcc 1497

<210> 357

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL1xCD19 HLLH

<400> 357

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
245 250 255

Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
260 265 270

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 358

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL2VH7xCD19 LHHL

<400> 358
gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
ctgagctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720
gtctcctccg gaggtggtgg atcccaggtg cagctgcagc agtctggggc tgagctggtg 780
aggcctgggt cctcagtgaa gatttcctgc aaggcttctg gctatgcatt cagtagctac 840
tggatgaact gggtgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg 900
cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca 960
gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg 1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac 1080
tactggggcc aagggaccac ggtcaccgtc tcctccggtg gtggtggttc tggcggcggc 1140
ggctccggtg gtggtggttc tgatatccag ctgacccagt ctccagcttc tttggctgtg 1200
tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt 1260

gatagttatt tgaactggta ccaacagatt ccaggacagc cacccaaact cctcatctat 1320

gatgcatcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctgggaca 1380

gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcactgtcag 1440

caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa 1494

<210> 359

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL2VH7xCD19 LHHL

<400> 359

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 360

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL2xCD19 HLHL

<400> 360

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780
gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
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tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
gactactggg gccaagggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140

ggcggctccg gtggtggtgg ttctgatatc cagctgaccc agtctccagc ttctttggct 1200

gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260

ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320

tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 1380

acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1440

cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 361

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL2xCD19 HLHL

<400> 361

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser

380

435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 362

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL2VH7xCD19 LHLH

<400> 362

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ctgagctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120

aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480

gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540

tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660

gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720

gtctcctccg gaggtggtgg atccgatatc cagctgaccc agtctccagc ttctttggct 780

gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840

ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900

tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 960

acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1020

cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt 1080

ggtggtggtt ctggcggcgg cggctccggt ggtggtggtt ctcaggtgca gctgcagcag 1140

tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200

tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggtcttgag 1260

tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaagggt 1320

aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380

gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440

tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

<210> 363

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL2VH7xCD19 LHLH

<400> 363

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp

145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
        435   440   445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
    450   455   460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
465   470   475   480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
                485   490   495

Ser Ser

<210> 364

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL2xCD19 HLLH

<400> 364
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgat atccagctga cccagtctcc agcttctttg 780
gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat 840
gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactcctc 900
atctatgatg catccaatct agtttctggg atcccaccca ggtttagtgg cagtgggtct 960

gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac 1020
tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa 1080
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag 1140
cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttcctg caaggcttct 1200
ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt 1260
gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag 1320
ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc 1380
ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctcctcc 1497

<210> 365
<211> 499
<212> PRT
<213> artificial sequence

<220>
<223> VH7VL2xCD19 HLLH

<400> 365

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
245 250 255

Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
260 265 270

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 366

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH7xCD19 LHHL

<400> 366
gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60

ctgacctgca gagccagttc aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120

aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480

gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540

tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660

gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720

gtctcctccg gaggtggtgg atcccaggtg cagctgcagc agtctggggc tgagctggtg 780

aggcctgggt cctcagtgaa gatttcctgc aaggcttctg gctatgcatt cagtagctac 840

tggatgaact gggtgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg 900

cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca 960
gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg 1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac 1080
tactggggcc aagggaccac ggtcaccgtc tcctccggtg gtggtggttc tggcggcggc 1140
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gatagttatt tgaactggta ccaacagatt ccaggacagc cacccaaact cctcatctat 1320
gatgcatcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctgggaca 1380
gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcactgtcag 1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa 1494

<210> 367
<211> 498
<212> PRT
<213> artificial sequence

<220>
<223> VL3VH7xCD19 LHHL
<400> 367

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
385 390 395 400

389
Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 368

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL3xCD19 HLHL

<400> 368
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780

gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840

tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt 900

tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960

gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020

gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080

gactactggg gccaagggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140

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acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1440

cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 369

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL3xCD19 HLHL

<400> 369

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
        115   120   125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
    130   135   140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145   150   155   160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
                165   170   175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
            180   185   190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
        195   200   205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
    210   215   220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225   230   235   240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
                245   250   255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
            260   265   270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
        275   280   285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
    290   295   300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
305   310   315   320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
                325   330   335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
            340   345   350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
        355   360   365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    370   375   380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala

385 390 392 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 370

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH7xCD19 LHLH

<400> 370

gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60

ctgacctgca gagccagttc aagtgtaagt tacatgaact ggtaccagca gaagccgggc 120

aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180

ttcagtggca gtgggtctgg gaccgactac tctctcacaa tcaacagctt ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480

gtaaggcagg cacctggaca gggtctggaa tggattggat acattaatcc tagccgtggt 540

tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660

gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720

gtctcctccg gaggtggtgg atccgatatc cagctgaccc agtctccagc ttctttggct 780

gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840

ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900

tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 960

acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1020

cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt 1080

ggtggtggtt ctggcggcgg cggctccggt ggtggtggtt ctcaggtgca gctgcagcag 1140

tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200

tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggtcttgag 1260

tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaagggt 1320

aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380

gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440

tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

<210> 371

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH7xCD19 LHLH

<400> 371

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr

100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 372

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL3xCD19 HLLH

<400> 372
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60

tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180

aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240

atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360

gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420

ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480

agagccagtt caagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600

agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgat atccagctga cccagtctcc agcttctttg 780
gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat 840
gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactcctc 900
atctatgatg catccaatct agtttctggg atcccaccca ggtttagtgg cagtgggtct 960
gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac 1020
tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa 1080
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag 1140
cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttcctg caaggcttct 1200
ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt 1260
gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag 1320
ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc 1380
ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctcctcc 1497

<210> 373

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL3xCD19 HLLH

<400> 373

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
245 250 255

Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
260 265 270

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 374

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH5/VL1 HLHL

<400> 374
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540

cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg 780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaaggtgtc ctgcaaggct 840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
ctggaatgga ttggatacat taatcctagc cgtggttata ctaattacgc agacagcgtc 960
aagggccgct tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
agcctgcgtt ctgaggacac tgcaacctat tactgtgcaa gatattatga tgatcattac 1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattcagat gacccagtct 1200
ccatctagcc tgtctgcatc tgtcggggac cgtgtcacca tcacctgcag agccagtcaa 1260
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1440
caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaa 1497

<210> 375

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH5VL1 HLHL

<400> 375

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
260 265 270

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
275 280 285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
290 295 300

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
305 310 315 320

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
355 360 401 365

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
385 390 395 400

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
405 410 415

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
485 490 495

Glu Ile Lys

<210> 376

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL1VH5 LHLH

<400> 376

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180

gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240

cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300

acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360

tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420

gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480

aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540

gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600

tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660

ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720

ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgacat tcagatgacc 780

cagtctccat ctagcctgtc tgcatctgtc ggggaccgtg tcaccatcac ctgcagagcc 840

agtcaaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900

tggatttatg acacatccaa agtggcttct ggagtccctg ctcgcttcag tggcagtggg 960

tctgggaccg actactctct cacaatcaac agcttggagg ctgaagatgc tgccacttat 1020

tactgccaac agtggagtag taacccgctc acgttcggtg gcgggaccaa ggtggagatc 1080

aaaggcgaag gtactagtac tggttctggt ggaagtggag gttcaggtgg agcagacgac 1140

gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaaggtgtcc 1200

tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260

ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacgca 1320

gacagcgtca agggccgctt cacaatcact acagacaaat ccaccagcac agcctacatg 1380

gaactgagca gcctgcgttc tgaggacact gcaacctatt actgtgcaag atattatgat 1440

gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 377

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL1VH5 LHLH

<400> 377

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

403

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
260 265 270

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe

404

340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
450 455 460

Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp
465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 378

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL1VH5 HLLH

<400> 378

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60

tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120

cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180

aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240

atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300

actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360

accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
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tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 1320
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 1380
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 1440
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 1497

<210> 379

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL1VH5 HLLH

<400> 379

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1   5   10   15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
            20   25   30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe

50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
260 265 270

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
305 310 315 320

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 380

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH5VL2 HLHL

<400> 380
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60

tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120

cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180

aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240

atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300

actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360

accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420

atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480

tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540

cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600

atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660

gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720

ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg 780

gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaaggtgtc ctgcaaggct 840

tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900

ctggaatgga ttggatacat taatcctagc cgtggttata ctaattacgc agacagcgtc 960

aagggccgct tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020

agcctgcgtt ctgaggacac tgcaacctat tactgtgcaa gatattatga tgatcattac 1080

tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140

actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gacccagtct 1200

ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa 1260

agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320

tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380

accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1440

caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaa 1497

<210> 381

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH5VL2 HLHL

<400> 381

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
260 265 270

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
275 280 285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
290 295 300

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
305 310 315 320

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
355 360 365

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
385 390 395 400

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
405 410 415

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
485 490 495

Glu Ile Lys

<210> 382

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL2VH5 LHLH

<400> 382
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atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180

gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240

cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300

acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360

tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420

gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480

aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540

gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600

tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660

ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720

ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgacat tgtactgacc 780

cagtctccag caactctgtc tctgtctcca ggggagcgtg ccaccctgag ctgcagagcc 840

agtcaaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900

tggatttatg acacatccaa agtggcttct ggagtccctg ctcgcttcag tggcagtggg 960

tctgggaccg actactctct cacaatcaac agcttggagg ctgaagatgc tgccacttat 1020

tactgccaac agtggagtag taacccgctc acgttcggtg gcgggaccaa ggtggagatc 1080

aaaggcgaag gtactagtac tggttctggt ggaagtggag gttcaggtgg agcagacgac 1140

gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaaggtgtcc 1200

tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260

ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacgca 1320

gacagcgtca agggccgctt cacaatcact acagacaaat ccaccagcac agcctacatg 1380

gaactgagca gcctgcgttc tgaggacact gcaacctatt actgtgcaag atattatgat 1440

gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 383

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL2VH5 LHLH

<400> 383

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
260 265 270

Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
290 295 300

413
Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
450 455 460

Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp
465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 384

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL2VH5 HLLH

<400> 384
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cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cattgtactg 780
acccagtctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gagctgcaga 840
gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
gggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020
tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag 1080
atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 1320
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 1380
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 1440
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 1497

<210> 385

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL2VH5 HLLH

<400> 385

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1   5   10   15

415

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
260 265 270

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr

290 295 300

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
305 310 315 320

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 386

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH5VL3 HLHL

<400> 386

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60

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cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180

aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240

atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300

actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360

accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420

atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480

tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540

cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600

atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660

gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720

ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg 780

gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaaggtgtc ctgcaaggct 840

tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900

ctggaatgga ttggatacat taatcctagc cgtggttata ctaattacgc agacagcgtc 960

aagggccgct tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020

agcctgcgtt ctgaggacac tgcaacctat tactgtgcaa gatattatga tgatcattac 1080

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actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gacccagtct 1200

ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca 1260

agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320

tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380

accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1440

caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaa 1497

<210> 387

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH5VL3 HLHL

<400> 387

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser

1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
260 265 270

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
275 280 285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
290 295 300

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
305 310 315 320

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
355 360 365

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
385 390 395 400

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
405 410 415

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
485 490 495

Glu Ile Lys

<210> 388

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL3VH5 LHLH

<400> 388
gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgacat tgtactgacc 780
cagtctccag caactctgtc tctgtctcca ggggagcgtg ccaccctgac ctgcagagcc 840
agttcaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900
tggatttatg acacatccaa agtggcttct ggagtccctg ctcgcttcag tggcagtggg 960
tctgggaccg actactctct cacaatcaac agcttggagg ctgaagatgc tgccacttat 1020
tactgccaac agtggagtag taacccgctc acgttcggtg gcgggaccaa ggtggagatc 1080
aaaggcgaag gtactagtac tggttctggt ggaagtggag gttcaggtgg agcagacgac 1140
gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaaggtgtcc 1200
tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260
ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacgca 1320
gacagcgtca agggccgctt cacaatcact acagacaaat ccaccagcac agcctacatg 1380
gaactgagca gcctgcgttc tgaggacact gcaacctatt actgtgcaag atattatgat 1440
gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 389

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL3VH5 LHLH

<400> 389

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1   5   10   15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
            20   25   30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
        35   40   45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
    50   55   60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65   70   75   80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
                85   90   95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
            100   105   110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
        115   120   125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
    130   135   140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145   150   155   160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
                165   170   175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
            180   185   190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
        195   200   205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
    210   215   220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225   230   235   240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
                245   250   255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
            260   265   270

Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
450 455 460

Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp
465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 390

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL3VH5 HLLH

<400> 390
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cattgtactg 780
acccagtctc cagcaactct gtctctgtct ccaggggagc gtgccacccт gacctgcaga 840
gccagttcaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
gggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020
tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag 1080
atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 1200
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 1320
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 1380
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 1440
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 1497

<210> 391

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL3VH5 HLLH

<400> 391

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

425

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
260 265 270

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
305 310 315 320

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 392

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH7VL1 HLHL

<400> 392
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg 780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaaggtgtc ctgcaaggct 840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
ctggaatgga ttggatacat taatcctagc cgtggttata ctaattacaa tcagaagttc 960
aaggaccgcg tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
agcctgcgtt ctgaggacac tgcagtctat tactgtgcaa gatattatga tgatcattac 1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140
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ccatctagcc tgtctgcatc tgtcggggac cgtgtcacca tcacctgcag agccagtcaa 1260
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1440
caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaa 1497

<210> 393

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH7VL1 HLHL

<400> 393

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1   5   10   15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
            20   25   30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
    50   55   60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85   90   95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
            100   105   110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115   120   125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
    130   135   140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145   150   155   160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
                165   170   175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
            180   185   190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
        195   200   205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
    210   215   220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225   230   235   240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser

428

245 250 255

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
260 265 270

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
275 280 285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
290 295 300

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
305 310 315 320

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
355 360 365

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
385 390 395 400

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
405 410 415

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
485 490 495

Glu Ile Lys

<210> 394

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL1VH7 LHLH

<400> 394
gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgacat tcagatgacc 780
cagtctccat ctagcctgtc tgcatctgtc ggggaccgtg tcaccatcac ctgcagagcc 840
agtcaaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900
tggatttatg acacatccaa agtggcttct ggagtccctg ctcgcttcag tggcagtggg 960
tctgggaccg actactctct cacaatcaac agcttggagg ctgaagatgc tgccacttat 1020
tactgccaac agtggagtag taacccgctc acgttcggtg gcgggaccaa ggtggagatc 1080
aaaggcgaag gtactagtac tggttctggt ggaagtggag gttcaggtgg agcagacgac 1140
gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaaggtgtcc 1200
tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260
ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacaat 1320
cagaagttca aggaccgcgt cacaatcact acagacaaat ccaccagcac agcctacatg 1380
gaactgagca gcctgcgttc tgaggacact gcagtctatt actgtgcaag atattatgat 1440
gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 395

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL1VH7 LHLH

<400> 395

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
                245   250   255

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
            260   265   270

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
        275   280   285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
    290   295   300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
305   310   315   320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
                325   330   335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
            340   345   350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
        355   360   365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
    370   375   380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
385   390   395   400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
                405   410   415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
            420   425   430

Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr
        435   440   445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
    450   455   460

Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp
465   470   475   480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
                485   490   495

Ser Ser

<210> 396

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL1VH7 HLLH

<400> 396

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
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cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cattcagatg 780
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gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
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tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag 1080
atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140
gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 1200
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cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 1320
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 1380
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 1440
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 1497

<210> 397

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL1VH7 HLLH

<400> 397

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1   5   10   15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
            20   25   30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
    50   55   60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85   90   95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
            100   105   110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115   120   125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
    130   135   140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145   150   155   160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
                165   170   175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
            180   185   190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
        195   200   205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
    210   215   220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
260 265 270

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
305 310 315 320

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 398

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH7VL2 HLHL

<400> 398
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
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cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg 780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaaggtgtc ctgcaaggct 840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
ctggaatgga ttggatacat taatcctagc cgtggttata ctaattacaa tcagaagttc 960
aaggaccgcg tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
agcctgcgtt ctgaggacac tgcagtctat tactgtgcaa gatattatga tgatcattac 1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gacccagtct 1200
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa 1260
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1440
caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaa 1497

<210> 399

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH7VL2 HLHL

<400> 399

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1   5   10   15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
            20   25   30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
    50   55   60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85   90   95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
            100   105   110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115   120   125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
    130   135   140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145   150   155   160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
                165   170   175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
            180   185   190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
        195   200   205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
260 265 270

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
275 280 285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
290 295 300

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
305 310 315 320

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
355 360 365

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
385 390 395 400

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
405 410 415

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val

485 490 495

Glu Ile Lys

<210> 400

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL2VH7 LHLH

<400> 400

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
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caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgacat tgtactgacc 780
cagtctccag caactctgtc tctgtctcca ggggagcgtg ccaccctgag ctgcagagcc 840
agtcaaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900
tggatttatg acacatccaa agtggcttct ggagtccctg ctcgcttcag tggcagtggg 960
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tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260
ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacaat 1320
cagaagttca aggaccgcgt cacaatcact acagacaaat ccaccagcac agcctacatg 1380
gaactgagca gcctgcgttc tgaggacact gcagtctatt actgtgcaag atattatgat 1440

gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 401

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL2VH7 LHLH

<400> 401

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln

440

195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
260 265 270

Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr
435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
450 455 460

Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp
465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 402

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL2VH7 HLLH

<400> 402
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
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cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cattgtactg 780
acccagtctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gagctgcaga 840
gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
gggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020
tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag 1080
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gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 1200
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 1320

aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 1380

atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 1440

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 1497

<210> 403

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL2VH7 HLLH

<400> 403

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
260 265 270

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
305 310 315 320

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 404

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH7VL3 HLHL

<400> 404
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60

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cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180

aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240

atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300

actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360

accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420

atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480

tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540

cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600

atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660

gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720

ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg 780

gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaaggtgtc ctgcaaggct 840

tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900

ctggaatgga ttggatacat taatcctagc cgtggttata ctaattacaa tcagaagttc 960

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tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140

actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gacccagtct 1200

ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca 1260

agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320

tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380

accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1440

caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaa 1497

<210> 405

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH7VL3 HLHL

<400> 405

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
260 265 270

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
275 280 285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
290 295 300

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
305 310 315 320

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
355 360 365

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
385 390 395 400

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
405 410 415

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
447 450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
485 490 495

Glu Ile Lys

<210> 406

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL3VH7 LHLH

<400> 406
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caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
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cagtctccag caactctgtc tctgtctcca ggggagcgtg ccaccctgac ctgcagagcc 840
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tggatttatg acacatccaa agtggcttct ggagtccctg ctcgcttcag tggcagtggg 960
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tactgccaac agtggagtag taacccgctc acgttcggtg gcgggaccaa ggtggagatc 1080
aaaggcgaag gtactagtac tggttctggt ggaagtggag gttcaggtgg agcagacgac 1140

gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaaggtgtcc 1200

tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260

ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacaat 1320

cagaagttca aggaccgcgt cacaatcact acagacaaat ccaccagcac agcctacatg 1380

gaactgagca gcctgcgttc tgaggacact gcagtctatt actgtgcaag atattatgat 1440

gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 407

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL3VH7 LHLH

<400> 407

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
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Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
            20   25   30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
        35   40   45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
    50   55   60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65   70   75   80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
                85   90   95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
            100   105   110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
        115   120   125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
    130   135   140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145   150   155   160

449
Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
260 265 270

Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr

450

435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
450 455 460

Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp
465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 408

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL3VH7 HLLH

<400> 408
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cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180

aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240

atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300

actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360

accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420

atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480

tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540

cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600

atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660

gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720

ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cattgtactg 780

acccagtctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gacctgcaga 840

gccagttcaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900

agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960

gggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020

tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag 1080

atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 1200

tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 1320

aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 1380

atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 1440

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 1497

<210> 409

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL3VH7 HLLH

<400> 409

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Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile

145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
260 265 270

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
305 310 315 320

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

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Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
        435                 440                 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
    450                 455                 460

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
465                 470                 475                 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
                485                 490                 495

Val Ser Ser
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